UNITED STATES OF AMERICA
BEFORE THE FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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In the Matter of:	FDA DOCKET: 00N-1571
	DATE: February 10, 2003
Enrofloxacin for Poultry: Withdrawal of Approval of Bayer Corporation's New Animal Drug Application (NADA) 140-828 (Baytril)	

Center for Veterinary Medicine's Response to Bayer and AHI's Motions to Strike Written Direct Testimony and Evidence

I. Introduction

On January 27, 2003, the parties to this hearing filed Motions to Strike Written Direct Testimony and Evidence.[1] By Order dated April 10, 2002, Responses to these Motions are due on or before February 10, 2003. CVM is today filing a Response to Bayer's Motion and respectfully requests that Bayer's Motion be denied.

At the outset, Bayer's Motion should be denied because that Motion represents improper testimony from counsel. In several portions of Bayer's Motion, counsel blithely recites "facts" with no references to existing testimony and/or exhibits. [For example, Bayer's Motion, p. 27: "...the fact is that ethnicity and income can have a large impact on factors that may influence

[1] On January 27, 2003, Bayer filed a lengthy Motion to Strike CVM's Written Direct Testimony and Evidence. On that same date, the Animal Health Institute filed a two sentence "adoption" of Bayer's Motion. For the purposes of this response, CVM's use of "Bayer" also includes the Animal Health Institute, where appropriate, and all requests for Bayer's Motion to be denied include the request for AHI's Motion to be similarly denied.

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chicken consumption, chicken preparation, access to health care and access to prescription medicine."; Bayer's Motion, p. 31: "A proper scientific study would include steps to correct for this factor. Because no such steps were taken here, the Poultry NARMS procedures fail to comport with accepted scientific procedure and must be excluded; Bayer's Motion, p. 33: "The treatment history of birds in the different programs could be very different because older birds (spent hens) are alive longer...."; Bayer's Motion, p. 48, "The CVM/Vose model is essentially just a ratio of two aggregate quantities (numbers of persons with fluoroquinolone-resistant *Campylobacter* infections and pounds of chicken meat with fluoroquinolone-resistant *Campylobacter*) that are not causally connected."]

Further, in one notable example, Bayer's counsel produces a chart entitled "International Travel by US Residents" [Bayer's Motion, p. 23]. This chart is not purported to be contained in any witness' testimony and, in fact, has not been represented by Bayer to be anywhere in the evidentiary record of this proceeding. This chart is a classic example of testimony by counsel and, for that reason alone, this motion should be denied.[2]

It should also be noted that Bayer's arguments with respect to Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), discussed below, are based primarily on improper testimony by counsel.

II. Reliability/Relevancy under Daubert Analysis

Bayer puts forward an argument that some of the data introduced by CVM is not reliable, citing Daubert, and its progeny. Daubert does not apply to a case before an Administrative Law Judge. See Consolidation Coal Company v. Director, Office of Workers' Compensation Programs, 294 F. 3d 885, 893 (7th Cir. 2002) ("...agencies are not bound by the evidentiary

strictures of *Daubert*....."). However, even if Daubert and progeny were binding in this proceeding, it is clear from a reading of these cases that the evidence submitted by CVM meets the Daubert standards for relevance and reliability.

The evidence will assist the Administrative Law Judge, as trier of fact, to understand or determine a fact in issue, and is relevant. The evidence is also reliable under a Daubert type evaluation of the evidence using some of the factors suggested by the Daubert Court along with other factors that the Administrative Law Judge should consider appropriate to evaluate in this case. The factors enumerated by Daubert[3] are not binding or exclusive. "But, as the Court stated in *Daubert*, the test of reliability is 'flexible,' and *Dabuert's* list of specific factors neither necessarily or exclusively applies to all experts or in every case. Rather, the law grants a district court the same broad latitude when it decides *how* to determine reliability as it enjoys in respect to its ultimate reliability determination." Kumho Tire Co. v. Carmichael, 526 U.S. 137, 141-142 (1999), citing General Electric Co. v. Joiner, 522 U.S. 136 (1997). Because a reliability evaluation is flexible under Daubert , the ALJ is free to take into consideration other important factors in deciding the reliability of proffered evidence.

CVM believes that certain factors enumerated by the Daubert Court as well as additional factors weigh heavily toward admissibility of the written direct testimony, data and documents submitted by CVM.

For example, with respect to the reliability of the epidemiological data (see Section VI below) there appears to be general acceptance within the relevant scientific community about the

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[2] The examples provided are just a sampling of improper testimony in the guise of counsel arguments. Additional examples of improper testimony appear at Bayer's Motion, pages 33, 38, 39, 40, 41, 42, 44, 46, and 59.

[3] The four factors set out by the Daubert Court are, "...whether the theory or technique in question can be (and has been) tested, whether it has been subjected to peer review and publication, its known or potential error rate and the existence and maintenance of standards controlling its operation, and whether it has attracted widespread acceptance within a relevant scientific community." Daubert, 509 U.S. at 580.

methodologies used. Similar types of studies using similar epidemiological methods are abundant. One need only peruse the docket of this hearing to find multiple studies using similar epidemiological methodologies. In fact, Bayer's own witness, Dr. Roger Feldman who was asked "to examine and testify about...epidemiology principles..." [Feldman WDT, B-1902, p. 3, Lines 20-21], attaches portions of what he describes as, "[T]he authoritative text *Field Epidemiology*, 2nd Edition; Oxford Press (2002); edited by Michael B. Gregg," [Feldman WDT, B-1902, p. 5, Lines 7-8]. The attached portion of that text, at Feldman WDT, B-1902, Attachment #1, p. 107-108 states:

> "...almost all studies conducted by field epidemiologists are observational studies, in which the epidemiologists document rather than determine exposures.
>
> You will likely conduct two types of epidemiological studies....In a *cohort* or *follow-up study*....In a *case-control study*, enrollment is based on the presence ("case") or absence ("control") of disease and the frequency of exposures in compared between the cases and controls. Each type of study has its strengths and limitation, but each has an important place in field investigations."

It is clear, from the above language, that case-control studies are a standard methodology used by epidemiologists that have an important place in field investigations, and any argument by Bayer that the listed exhibits are not reliable based on methodology used is easily rejected.

Additionally, most data subject to Bayer's Motion were generated apart from the hearing process, as a pursuit of scientists working on their own research or research in conjunction with governmental agencies (both domestic and foreign). This factor weighs heavily in favor of reliability and admissibility. On remand, the 9th Circuit Daubert panel said, "[O]ne very significant fact to be considered is whether the experts are proposing to testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions expressly for purposes of testifying." Daubert II, 43 F.3d 1311, 1317 (9th Cir. 1995).

Further, CVM believes that much of the data in question have been developed and presented in an open and transparent process. Many of these data are contained on CVM's (or another relevant government agency's) website, and other data have been the subject of public meetings and have been published in the Federal Register. For example, CVM's Risk Assessment was posted on CVM's internet homepage, including the downloadable version of the model used, and the Risk Assessment was the subject of a public meeting where comments were accepted. [Vose WDT, G-1480, p. 6, Lines 25-36].

Finally, contrary to Bayer's argument [Bayer's Motion, p. 53] that the reliability of certain studies is "suspect" since they were not published in peer-reviewed scientific journals, many of these studies were, in fact, peer-reviewed or subject to equivalent processes. For instance, the testimony submitted by Dr. Kirk Smith from the Minnesota Department of Health (G-1473) is based on and related to an epidemiological study conducted by Dr. Smith and colleagues and peer-reviewed and published in the New England Journal of Medicine (G-589). And, Dr. Neimann's analysis, as part of a Ph.D. thesis (B-561), was likely subjected to the detailed review normally accorded such doctoral requirements. In addition, most of the specific epidemiological documents that Bayer objects to in its Motion have multiple authors listed, each providing a level of oversight and "peer" review. With that said, and while peer-review and publication certainly lend credence to studies, the Daubert Court did not rule that studies are "suspect" if they have not been peer-reviewed.

Below, in Sections III through IX of this response, CVM has included specific arguments relevant to each category of data that Bayer has questioned, and has included, as part of Section XI, a point-by-point response to Bayer's Appendix H, which Bayer describes as a Master List of

Bayer's Appendices A-G to Bayer's Motion to Strike CVM's Written Direct Testimony and Evidence.[4]

At this point, and before CVM lays out specific arguments for denying Bayer's Motion, it should be repeated and stressed that Bayer's Daubert-type reliability arguments substantially rely on improper testimony by counsel, and CVM is being forced to respond to "factual" statements unsupported by disclosed references to the record. It is wholly inappropriate to expect CVM or the Administrative Law Judge to read through the entire record to find any support, if it exists, for Bayer's contentions. CVM continues to object to this tactic and requests that Bayer's Motion to Strike be denied in its entirety.

III. Reliability under FDA Guidelines for Ensuring Quality of Information

Bayer's Motion, pages 14 to 19, seeks to strike testimony and evidence submitted by CVM through FDA's Guidelines for Ensuring the Quality of Information Disseminated to the Public ("FDA Guidelines" or "data quality guidelines"), 67 Fed. Reg. 61343 (Sept. 30, 2002).[5] CVM believes that this administrative hearing does not afford Bayer any opportunity to use the FDA Guidelines to challenge CVM's testimony or evidence. For the reasons discussed below, no testimony or evidence should be stricken on these grounds.

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[4] CVM adapted Bayer's chart by deleting the last column ("Reason to Strike") and replacing it with a column titled "Reason to Deny Bayer's Motion to Strike." The adapted chart is included in Section XI of this Response.

[5]The FDA Guidelines were issued in accordance with guidelines issued by the Office of Management and Budget (called, "Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies"), which implement section 515 of the Treasury and General Government Appropriations Act for Fiscal Year 2001 (Pub. L. 106-554; H.R. 5658).

Bayer also argues that CVM has not complied with similar data quality guidelines issued by CDC. Contrary to Bayer's assumption, CVM is not bound by CDC's data quality guidelines. Overlooking the fact that CDC's guidelines are non-binding (and, therefore, do not even bind CDC), the scope of CDC's guidelines is limited to information disseminated by CDC. And, even if CVM were covered by CDC's data quality guidelines, those guidelines are inapplicable to this proceeding for the same reasons demonstrating the inapplicability of the FDA Guidelines.

First, the FDA Guidelines do not create or confer any rights, nor do they operate or bind FDA or the public. The non-binding nature of the FDA Guidelines is explained on the first page of the document, which says:

> This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

The FDA Guidelines confer no rights on Bayer.

Second, Bayer attempts to transform the data quality guidelines from an elucidation of FDA's "current thinking" on ensuring the quality of disseminated information to a test governing the admissibility of expert testimony in this hearing. The FDA Guidelines do not even purport to set forth a standard for excluding expert testimony in an administrative proceeding. Bayer's strategy to use the data quality guidelines for this purpose must fail.

Third, should Bayer wish to seek relief under the FDA Guidelines, Bayer must follow the procedures set forth in the FDA Guidelines.[6] The FDA Guidelines explain the administrative mechanisms that are in place to enable members of the public to seek correction of information maintained and disseminated by FDA that they believe does not comply with the data quality guidelines. The administrative procedure contained in the FDA Guidelines describes FDA's intent to use existing mechanisms to address requests for information correction ("complaints") from the public. The procedures for submitting complaints, FDA's response to complaints, and

[6]CVM makes no assessment here of the propriety of a submission by Bayer or AHI of a complaint, pursuant to the FDA Guidelines, during the pendency of this administrative hearing on any issue related to, or any data, evidence, or testimony relied on in, the hearing.

requests for reconsideration are outlined in the data quality guidelines. Any agency response that may be afforded to Bayer pursuant to the FDA Guidelines is limited by the guidance itself.[7]

Fourth, assuming that it is permissible for Bayer (i.e., Bayer itself, or through AHI) to submit a complaint, pursuant to the FDA Guidelines, during the pendency of this administrative hearing, on hearing-related issues, Bayer has already done so. On January 23, 2003, AHI submitted a request for information correction to FDA under the FDA Guidelines. AHI's complaint focuses on the same data and employs a similar rationale in its critique of those data as does Bayer's Motion to Strike.[8] Assuming the propriety of AHI's submission, FDA's review of AHI's complaint will conform to the administrative procedure outlined in the FDA Guidelines.

Because the FDA Guidelines are non-binding and non-controlling, CVM believes it is unnecessary to respond substantively to arguments in this part of Bayer's Motion. More importantly, because of the pending AHI submission pursuant to the FDA Guidelines, CVM believes it would be inappropriate to provide a substantive response here to Bayer's challenges. It is not appropriate to preempt the role of CVM in this matter. To be clear, CVM counsel is not suggesting that the ALJ is precluded from considering the quality of the data submitted by CVM

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[7]The FDA Guidelines state that a complaint should include, among other things, the specific reasons the complainant believes specified information does not meet applicable data quality guidelines; the specific recommendations for correcting the information; and a description of how the complainant is affected by the information error. FDA's review of the information submitted and its determination whether a correction is warranted and, if so, how that correction will be made, are outlined in the FDA Guidelines.

[8]In its complaint, AHI supports its allegation that the Campylobacter Resistance Risk Assessment (i.e., the "CVM / Vose Risk Assessment") is incomplete and unreliable by incorporating into its complaint all of the written direct testimony submitted by the respondents' expert witnesses in this hearing.

AHI also submitted a complaint to CDC (originally submitted on December 13, 2002, and amended on or about January 10, 2003), alleging data inaccuracies in various CDC abstracts and presentations. The data and statements to which AHI object are: (1) the NARMS data and the CDC sentinel county study to support the rising incidence of fluoroquinolone resistant Campylobacter; (2) the Mead study to support the estimated annual incidence of 2.4 million cases of Campylobacter infection in the United States; and (3) the duration of diarrhea analyses of the CDC case control study data to support the longer duration of illness associated with fluoroquinolone resistant Campylobacter infection. AHI relies on written direct testimony submitted by its and Bayer's expert witnesses in this hearing to justify its allegations.

as testimony and exhibits in this hearing. Rather, CVM's position is that the ALJ's evaluation of expert testimony in this hearing should not be based on the FDA Guidelines. Any argument put forth by Bayer relying on the FDA Guidelines should be disregarded, and no testimony or evidence should be stricken on that basis.

IV. NARMS Data are Relevant and Reliable

Bayer's Motion, pages 19 to 35, seeks to strike all NARMS data and all testimony and documents relying on NARMS data. None of the reasons advanced by Bayer justifies striking these data, testimony, or documents. First, in seeking to strike the evidence, part of Bayer's justification amounts to testimony by Bayer's counsel.[9] As discussed earlier in CVM's Response, such testimony by counsel is improper and cannot be used to support a motion to strike. Second, many of the purported "flaws" in NARMS raised by Bayer are irrelevant, immaterial, or speculative. [See CVM's Motion to Strike, at 71 to 72 (critiquing the testimony of Bayer witness Bradley DeGroot)]. Third, Bayer muddies the determination of admissibility with an assessment of evidentiary weight. To the extent that any purported "flaw" raised by Bayer is relevant to the issue in this hearing, it is more properly vetted in cross-examination or rebuttal testimony, if permitted.

Finally, Bayer's attempt to have the trier of fact disregard animal and human NARMS data in their entirety is premised on Bayer's artificial deconstruction of the NARMS program. As explained in the Center's written direct testimony, NARMS data are part of the information evaluated by CVM during the process leading to its decision to withdraw the approval for Baytril. [See, e.g., Tollefson WDT, G-1478: p. 6, lines 12 – 16; p. 14, line 45 – p. 15, line 12; p. 16, lines 27 – 34; p. 18, lines 30 – 34; p. 19, line 18 – p. 20, line 5]. CVM evaluated data from

[9]Even where Bayer could have explicitly referred, with a citation, to the written direct testimony of its experts for the arguments advanced, it did not; Bayer, rather than its experts, testifies.

the NARMS program in light (not in lieu) of existing epidemiological and microbiological information and relied on NARMS in conjunction with other available data, studies, and analyses. The context in which CVM evaluated and relied on NARMS is evident not only from the testimony of Dr. Tollefson, but from information in addition to NARMS that is presented in the many other testimonies supporting CVM's position in this hearing. Bayer's review of NARMS in isolation, therefore, is unhelpful and irrelevant.

A. Human NARMS

1. Reliability - Human NARMS

Bayer contends that the data from human NARMS are unreliable because of alleged issues of confounding, protocol adherence, and representativeness.[10]

Confounding: Bayer's argument that NARMS is confounded by international travel and prior antibiotic use is unavailing. Bayer's Motion, pages 22 to 23, consists of testimony by Bayer's counsel, which is improper. The figure titled, "U.S. Resident International Overnight Trips: 1990 - 2000," described on page 22 and shown on page 23 has not been properly placed into evidence. There is no citation to the record for this testimony and CVM is not aware that the information can even be found elsewhere on the Docket. This section of Bayer's Motion should be ignored.

Further, as addressed by CVM through its witness testimony, the primary purpose of NARMS is to monitor antimicrobial resistance among foodborne enteric bacteria, including Campylobacter. [See Angulo WDT, G-1452: p. 3, L18 - L19; Tollefson WDT, G-1478: p. 5,

[10]Bayer also mentions in its introductory paragraphs, pages 20 to 21, that there is "[n]o control for outliers" and "[n]o baseline data." Bayer offers neither a complete explanation in the introductory paragraphs or elsewhere of these statements nor any relevant citations to the record. Bayer's suggestion that there is no control for outliers is flatly contradicted by the testimony of Dr. Angulo describing the multivariate logistic regression, which controlled for site-to-site variation. [See Angulo WDT: p. 8, L23 - L47]. Regarding baseline data, it is unclear from Bayer's Motion whether Bayer is referring to human or animal NARMS. In any event, the unreliability allegation must fail because it does not even call into question the NARMS data.

L29 - L32]. As explained in CVM testimony, NARMS detects emerging resistance and guides studies that evaluate where and how people become infected with resistant foodborne bacteria. [See Angulo WDT: p. 3, L19 - L21; Tollefson WDT: p. 5, L36 - L37]. NARMS data are used by the CDC and state health departments to investigate outbreaks caused by particular bacteria, conduct other studies to better understand the circumstances under which resistant bacteria arise and spread, and guide efforts to mitigate antimicrobial resistance. [See Angulo WDT: p. 3, L21 - L24].

NARMS is an active laboratory-based public health surveillance system. [See Angulo WDT: p. 4, L37 (describing FoodNet, within which NARMS is conducted)]. Public health surveillance systems are not designed to collect data on risk factors (e.g., international travel, prior antibiotic use). These systems serve as a platform for additional analytic epidemiological studies, such as the CDC case-control study and analyses conducted therein. [See CVM's Motion to Strike, at 71 to 72 (testimony of Bayer witness Bradley DeGroot)]. The "confounding" raised by Bayer, which is called "sampling bias" by DeGroot, is neither. These points are standard issues of generalizability that occur in most public health surveillance programs, which are typically based on existing clinical diagnostic laboratory data.

Even if Bayer's improper testimony and irrelevant, unreliable arguments were not discounted, it is possible, contrary to Bayer's opinion, to estimate the impact, if any, of limitations on generalizability. Further, relevant analytic epidemiological studies (e.g., the CDC case-control study) have been conducted, which by definition and design are suited to evaluate risk factors and adjust for confounding variables. A more detailed evaluation of data generalizability is more properly accomplished by expert testimony on cross-examination and rebuttal, if permitted. Similarly, a more searching inquiry into an expert's method and scope of

reliance on the data is best achieved under circumstances that permit the expert to provide the answers.

Protocol Adherence: Bayer's alleged "flaw" that NARMS does not adhere to its own methodology is based solely on Bayer's unproven assertion that there has been "[h]ighly variable compliance" by the state public health departments. Bayer's unsubstantiated conclusion is premature, resulting from (1) a misunderstanding of sentinel clinical laboratories within participating states versus participating state health department laboratories, and (2) an invalid assumption that all samples submitted were susceptibility tested or were part of a final dataset used for analysis. [See CVM's Motion to Strike, at 71 (testimony of Bradley DeGroot)]. By maintaining that it is "impossible to reconcile the data with any expected rate of error," Bayer appears to believe that data quality and protocol compliance are incapable of evaluation. If Bayer were correct that the degree of compliance cannot be determined, it would seem unlikely that Bayer would have information to allege that protocol compliance issues existed. A more detailed evaluation of data quality and protocol compliance is more properly accomplished by expert testimony on cross-examination and rebuttal, if permitted.

Representativeness: Bayer contends that NARMS does not represent the experience of the U.S. population because it is based on (1) ill people seeking medical care, (2) a one-sample-per-week sampling scheme, and (3) non-representative selection of participating states. Bayer's support for these contentions consists of improper testimony and irrelevant, unreliable arguments.

There is no dispute that NARMS is based on ill people seeking medical care. The surveillance program is based on existing clinical diagnostic laboratory data from ill people

seeking medical care. Thus, ill people seeking medical care is the population of interest in human NARMS.

Bayer's Motion, pages 25 to 26, consists of testimony by Bayer's counsel, which is improper. Bayer claims that NARMS is not based on proper epidemiological surveillance. These pages, which describe Bayer's analysis of the impact of a one-sample-per-week sampling scheme on data collected in NARMS, are without citation to expert testimony in the evidentiary record to substantiate the analysis. This testimony is impermissible, and this section of Bayer's Motion should be ignored.

Next, Bayer argues that not all states participate in NARMS and that the "set of states from which the samples are taken does not represent the general US population." According to Bayer, "campylobacteriosis and resistance are extremely variable among FoodNet sites." First, it is not disputed that some states do not participate in NARMS. NARMS is a sentinel system, which by definition calls for sites to be selected from a universe of sites so that they can participate as sentinels. Second, Bayer's allegation is vague. Bayer does not show, or even allege, that the states selected do not adequately represent any expected variability across the nation. So, it is unclear what effect Bayer believes the selected set of states has on infection and resistance rates.

The three representativeness factors raised by Bayer are part of the standard issue of generalizability addressed above. Further, even if, for example, the selection of states is shown not to represent the "experience" of the US population, an expert remains entitled to rely on these data to form an opinion. Data may be relied on in whole, in part, or in conjunction with other data and studies, or for certain (but not all) conclusions. Again, as suggested above, a more

detailed evaluation of and searching inquiry into these issues are well-suited to expert testimony on cross-examination and rebuttal, if permitted.

2. Relevancy - Human NARMS

Bayer repeats many of the same allegations regarding the reliability of NARMS in arguing about the relevancy of NARMS. The responses to the reliability arguments equally apply to the same issues appearing as relevancy arguments. To the extent that Bayer presents new allegations, they are equally invalid as the repetitive allegations.

Representativeness: Bayer argues, again, that NARMS is "not representative of the national population" for reasons of demographic variation (ethnicity and income), foreign travel, state participation, and sample selection.

Bayer argues that the demographics of NARMS is not representative of the U.S. In so arguing, Bayer misleadingly portrays the methods of a study, cited in the testimony of Dr. Angulo, that assessed the comparability of FoodNet and U.S. populations using 1996 data. [See Angulo WDT: p. 4, L6 - L34]. The study, which is in the evidentiary record of this hearing (G - 769), describes the methodology used and speaks for itself. Bayer, however, provides no citation for why Bayer concludes that the study assessed the data in a way that neither the study itself nor the witness testifying about the study even suggests.

Bayer's Motion, pages 28 to 29, consists of testimony by Bayer's counsel, which is improper. In these pages, Bayer presents an analysis of an "INCOME" variable (as well as other variables) comparing Connecticut and "other states." It is not clear what data were used and how the comparison was made. The discussion is without citation to expert testimony in the evidentiary record to substantiate the analysis. This testimony is impermissible and should be ignored. Moreover, Bayer's allegation is vague. Bayer does not show, or even allege, that the

states participating in NARMS do not adequately represent any expected variability in income (and in the other variables assessed by Bayer) across the nation. So, it is unclear what effect Bayer believes the selected set of states has.

Penultimately, Bayer cites to B-39 to support its argument that, because Wisconsin is not one of the states participating FoodNet (and NARMS), NARMS is not representative of the nation. It is unclear from the reference, B-39, a three-page study comparing "filtration" with "selective media" for the isolation of Campylobacter, that the samples analyzed were from Wisconsin. Even if they were, Bayer's hypothesis that "[o]ther states may have had similarly high rates [to Wisconsin] in the late 1980s and early 1990s" is unsupported by any citation to the evidentiary record.

Ultimately, Bayer cites to G-644, dubs the author a "neutral observer" and concludes that the author believes that human NARMS is not adequately generalizable. However, in the sentence that appears immediately after the one quoted by Bayer, the author states, "The human sampling is fairly representative of the human population."

Bayer simply disagrees with the conclusion of Dr. Angulo regarding the comparability of FoodNet and the U.S. population. This disagreement without more is not a sufficient reason to strike NARMS data, documents, and testimony.

On the issue of sample selection, Bayer asserts that the submitting laboratories are not prevented from choosing "'interesting' but non-representative samples" for inclusion in NARMS. What would cause one stool sample to look more interesting than another stool sample in the pool is left to the imagination. This strange accusation of "uncontrolled selection" is unproven, and there is no suggestion by Bayer that it has actually occurred.

B. Animal NARMS

1. Reliability - Animal NARMS

Bayer contends that data from animal NARMS are unreliable because of the isolation methods used and because year-to-year comparisons cannot be made.[11]

Isolation Methods: Bayer attempts to substantiate its claim that there is uncertainty in animal NARMS data from the use of selective media by relying on a report by Margie Lee that Bayer submitted as part of its witness testimony. CVM has moved to strike the report and related testimony on the ground that they are unreliable. [See CVM's Motion to Strike, at 71]. Moreover, Bayer's discussion of Dr. Lee's report, which is not published or peer-reviewed, presents only part of her results, i.e., those results that showed a difference between culture procedures on one farm. Dr. Lee's report, however, states that she cultured isolates from not one but three commercial farms. Bayer's testimony on Dr. Lee's report, as well as the report itself, are not of sufficient reliability to be included in the evidentiary record and are less capable of serving as a legitimate reason to strike testimony.

Bayer also considers that an abstract by USDA's Paula Fedorka-Cray comparing "spin enrichment" and "micro-well dilution" isolation methods gives reason to strike animal NARMS. The impact, if any, of Dr. Cray's results is more properly examined and evaluated by expert testimony on cross-examination and rebuttal, if permitted.

Trends: Again citing to the "neutral [observer]" in G-644, Bayer makes an extravagant exaggeration that the author "rejected" the NARMS program. First, Bayer's allegation is patently unsupported as evident from the author's own words, which state simply, "The animal sampling

[11]Bayer also mentions in its introductory paragraphs, pages 20 to 21, that there is "[m]ultiple counting (and hence over-representation)" of contaminated animal facilities, which bias the data. After testifying, Bayer shows no proof that "multiple counting" ever happened and, even if it had, it is not clear how it would bias resistance results. Similarly vague and unsubstantiated is Bayer's assertion that NARMS is unsound because it does not provide an estimate of the "quantitative extent of exposures." These reasons do not provide any justification for striking animal NARMS data, documents, and testimony.

might introduce some selection bias." Second, even if Bayer's interpretation were true, which it is not, Bayer's representation that the author, i.e., one person, is the "scientific community" is a hyperbole. Bayer provides no valid reason for why animal NARMS should be stricken.

2. Relevancy - Animal NARMS

Bayer argues that animal NARMS does not represent the poultry that is consumed by the general public. As CVM's testimony clearly presents, and as Bayer's Motion acknowledges, CVM experts are aware of the different sources of samples in animal NARMS. [See, e.g., Tollefson WDT: p. 12, L2 – 7]. Despite Bayer's contention, different sampling sources is not indicative of a "lack of 'fit'" that warrants the exclusion of animal NARMS. Moreover, as explained in CVM witness testimony, [see, e.g., Tollefson WDT: p. 12, L8 - p. 3, L28], NARMS also conducts studies on retail meat. These studies assist in the interpretation of animal data. "Retail food represents the point of exposure that is closest to the consumer and, when combined with data from slaughter plant samples, provides a more representative picture of the prevalence of resistant pathogens in products derived from food-producing animals." [Tollefson WDT: p. 12, L10 – 14].

C. NARMS Usage

Bayer maintains that CVM is using human and animal NARMS for purposes beyond which they were designed. Apparently, Bayer misunderstands how CVM uses data from the NARMS program. Additional clarification can be provided during any cross-examination and rebuttal permitted in this hearing. Moreover, CVM's use of the data in connection with meeting its burden in this proceeding is an important consideration. The connection should be permitted to continue to develop during the course of the hearing.

D. Admissibility

Bayer argues that human and animal NARMS do not meet the criteria for admissibility because they do not comport with FDA Guidelines and Daubert standards. The FDA Guidelines are unhelpful to Bayer in this setting. Moreover, Bayer's Daubert argument fails. NARMS is relevant, reliable, and scientifically sound. The issues raised by Bayer through testimony by counsel should be disregarded; the remaining issues are not properly dealt with by motion to strike. The evidence should be heard by the trier of fact in this proceeding and then weighed accordingly. For all of these reasons, human and animal NARMS data, testimony, and documents should not be stricken from the evidentiary record, and this part of Bayer's Motion should be denied in its entirety.

V. CVM/Vose Risk Assessment is Relevant and Reliable

Bayer's Motion at pp. 36-50 seeks to strike the risk assessment, The Human Health Impact of Fluoroquinolone Resistant Campylobacter Attributed to the Consumption of Chicken ["Campylobacter Risk Assessment"], that Bayer and other members of the new animal drug industry requested be conducted. [Tollefson WDT at 15, ¶ 39]. None of the reasons Bayer advances justifies striking this risk assessment. This antimicrobial resistance risk assessment is indeed different from a microbial risk assessment, as Bayer observes, but it was different for a scientifically appropriate reason, as explained in the Campylobacter Resistance Risk Assessment, G-953, and in the written direct testimony of Dr. Bartholomew and Dr. Vose.

Bayer's mischaracterization of an FDA guideline on dissemination of information as including "Controlling Standards" for FDA risk assessments should not mislead the Administrative Law Judge. At page 36 of its Motion to Strike, Bayer acknowledges that a recent FDA document is a Guideline, but misnames it "Controlling Standards." The

difference is significant, and significantly, is not revealed in Bayer's Motion. Those guidelines were first published in 2002, well after the Campylobacter Risk Assessment was completed, and after it was published in final form in January, 2001 [G-953].

Bayer's cite to these non-binding guidelines is a web link [Bayer Motion, p. 15, n. 4] not an exhibit number, as these guidelines are properly not a part of this record, nor are they, as Bayer would have the Administrative Law Judge believe, "controlling." Bayer's arguments [Bayer's Motion, at 36-39] based upon these non-binding guidelines are thus hollow.

Perhaps conceding that these guidelines do not justify striking this risk assessment, Bayer next assails them with the similarly unavailing allegation that the Risk Assessment made public in October 2000 and in final form in January 2001 does not adhere to another FDA Draft Guidance, published September 6, 2002. [Bayer's Motion, p. 39]. Again, Bayer does not cite to any exhibit number for the Draft Guidance. No matter; it is a Draft Guidance, published almost two years after the Risk Assessment was released. Bayer's argument should not be heard in this Motion; a Draft Guideline does not require the striking of a risk assessment prepared well before the Draft Guidance was published.

Continuing to flail against the Campylobacter Risk Assessment, Bayer, next truthfully (but misleadingly) notes that the Campylobacter Risk Assessment does not "specify additional studies not used...and the rationale of why they were not used" [Bayer's Motion, p. 40]. For support for this contention, Bayer cites three studies that are in this record, that the Campylobacter Risk Assessment did not specify: G-228, G-185, and G-1711. A glance at each of these studies reveals that **none of them had been published at the time the Campylobacter Risk Assessment was conducted**. G-228 is an abstract that was revised in October 2000, the same month the Campylobacter Resistance Risk Assessment was released. G-185 was published

in 2001. G-1711 was accepted for publication in June 2001. Bayer confirms its reliance on post-assessment studies again on page 43 of its Motion, where it claims that "...studies **since 2000** have documented the reduced risk of campylobacteriosis associated with chicken consumption and have implicated other sources..." [emphasis added]. So, even if the conductors of the 2000 Campylobacter Risk Assessment had the foreknowledge presumed by Bayer to anticipate these publications, the "rationale" for not including these publications would have been: "We do not include data, in producing this risk assessment, that are not available to us now, that might be available in the future." The "failure" to explain why they did not include such data, is no reason to strike the Campylobacter Risk Assessment.

So Bayer swings again at the Campylobacter Risk Assessment, [Bayer's Motion, p. 41] saying of the risk assessment that one could equally well divide the number of flat tires per year in each FoodNet area by quantities of orange juice consumed there to establish a relation between those numbers and orange juice consumption. Such an entertaining image incorporates the erroneous pretense that health effects of fluoroquinolone-resistant *Campylobacter* are as unrelated to the chicken that carry those *Campylobacter* as orange juice consumption is to flat tires. But Bayer's own witnesses have testified that *Campylobacter* is widespread in poultry [Newell WDT at 5]; that use of fluoroquinolone in poultry selects for resistant Campylobacter [Newell WDT at 11, 16; Van den Bogaard WDT at 3, 5, 7]; that people eat poultry, [Haas WDT at 12 - 13]; that people acquire resistant strains of *Campylobacter* via food, [Newell WDT at 20 – 21] and that treatment is compromised when pathogens are attacked with antimicrobials to which they are resistant [Newell WDT at 37]. This Bayer argument (like the other arguments that precede it) provides no support for Bayer's motion to strike the Campylobacter Risk Assessment. So Bayer's tire analogy is flat, but educational: it distinguishes between contrived

relationships and real ones, those based upon the existence of a scientifically-established basis. Witnesses for both parties to this hearing have testified to the elements of the scientific bases for the relationship described in the Campylobacter Risk Assessment. The Center urges the Administrative Law Judge to deny Bayer's motion to strike it.

Bayer goes on to base its motion to strike the Campylobacter Risk Assessment on Bayer's presumption that the risk assessment will be shown to be "invalid, inaccurate and in conflict with available data". [Bayer's Motion at 42]. But determinations of validity, accuracy and conflict are for the Administrative Law Judge to make, based in part on the evidence which Bayer presents, after any cross-examination that may be permitted of witnesses presented by both parties to the hearing. The Center notes that the contrasts noted in the paragraphs above demonstrate that Bayer's assertions of "invalidity" should be tested against the evidence. To this end, the Campylobacter Risk Assessment should not be stricken.

Bayer's claim of "inaccurate data" [Bayer's Motion, p. 44] is an opportunity for Bayer to present proof in its testimony and to brief its interpretation after the hearing. Bayer's presumption there, that its view of the data is the only correct one, is a reason Bayer wanted this hearing, not a basis for striking testimony.

Bayer correctly notes [Bayer's Motion, p. 45 and 49] that a risk assessment designed to assess a particular risk is not necessarily going to capture other risks, nor will it measure any alleged benefits of the risk-inducing article or practice. This reveals the focus of a specialized risk assessment, but is not a defect, nor a justification to strike. As the Administrative Law Judge has previously determined, the issue for this hearing is whether Baytril has been shown to be safe, not whether it makes money or accomplishes other good things for Bayer and for the Animal Health Institute or even whether it does other good things for the public. If Baytril is

revealed by this hearing not to have been shown to be safe, then its approval must be withdrawn, and Bayer will be free to reapply if and when it has adequate data to attempt again to prove Baytril's safety. If Bayer wishes to re-apply with such additional claims of efficacy as a claim that Baytril use will reduce the number and morbidity of human *Campylobacter* infections of those that are conveyed to humans by infected chickens, it would be free to do so. Meanwhile, the Center urges the Administrative Law Judge to deny Bayer's motion to strike the Campylobacter Risk Assessment, based on Bayer's contention that the risk assessment for one risk did not include all the risks, or any of the benefits of continuing use of Baytril in poultry.

Bayer argues [Bayer's Motion, at 47-49] that the Campylobacter Risk Assessment model has not been tested or validated, and that it is not generally accepted in the scientific community. The hearing, including any cross examination permitted, is the proper forum for Bayer to attempt to establish support for these arguments, and these arguments of Bayer can properly be made in its post-hearing brief, when they can be tested by comparison to any references to appropriate citations to the record, evaluated in the light of what is developed in cross examination. This hearing is a part of that testing, The testimony, once it is all said and done, will permit the Administrative Law Judge to assess the Campylobacter Risk Assessment model's acceptance better than reliance on the Center's and Bayer's respective confidence in our assertions about it. Though Bayer concedes that the Campylobacter Risk Assessment was reviewed by outside experts and recommendations solicited from sources outside the Center, and that Bayer understands that it will be published [Bayer's Motion, pp. 46-47]; Bayer argues that more review is needed. That "more" is this hearing, where Bayer can present it's evidence, followed by its arguments, if by then they are supported by citations to evidence in the record. Bayer has

already stipulated the "causal connection" it declares missing at page 48 of its Motion to Strike, in Revised Joint Stipulations 1, 3, 7 and 45:

> 1. Fluoroquinolone resistance develops in *Campylobacter* as a spontaneous genetic mutation within a *Campylobacter* population and is not as a result of exposure to fluoroquinolones. Fluoroquinolone exposure then can select for resistant *Campylobacter.*
>
> 3. In late 1993 or early 1994, before fluoroquinolones were approved for use in chickens and turkeys, CVM management understood and accepted that if fluoroquinolones were used in chickens and turkeys, the potential existed for fluoroquinolone-resistant *Campylobacter* to be transferred from chickens and turkeys to humans and contribute tot he development of fluoroquinolone-resistant *Campylobacter* infections in humans.
>
> 7. Fluoroquinolone use in chickens and turkeys can act as a selection pressure for fluoroquinolone-resistant bacteria in the chicken and turkey digestive tract.
>
> 45. The use of enrofloxacin in chickens and turkeys can exert a selection pressure that can lead to fluoroquinolone resistance.

Finally, it is useful to note that the Campylobacter Risk Assessment meets a Daubert type reliability evaluation. The Risk Assessment was conducted as part of CVM's activities apart from this hearing. Further, CVM believes that much of the data in question have been developed and presented in an open and transparent process. Many of these data are contained on CVM's (or other relevant government agency's) website, and other data have been the subject of public meetings and have appeared in the Federal Register. For example, CVM's Risk Assessment was posted on CVM's internet homepage, including the downloadable version of the model used, and the Risk Assessment was the subject of a public meeting where comments were accepted. [Vose WDT, G-1480, p. 6, lines 25-36] While this may not be a formal peer review, it serves a similar purpose. Further, as indicated earlier, while peer review may help make data more reliable, the lack of peer review does not make the data somehow "suspect."

VI. Epidemiological Data are Relevant and Reliable

Bayer makes several arguments with respect to studies[12] showing an increased duration of diarrhea from fluoroquinolone-resistant Campylobacter compared with fluoroquinolone-sensitive Campylobacter. In sweeping statements, Bayer claims, "[T]he cited studies, however, are unreliable and incorrect because they fail to use generally accepted epidemiological methods in analyzing the data. Moreover, many have not been peer-reviewed or published. As such, the studies and all testimony relying on the studies should be excluded." (Footnote omitted) [Bayer's Motion, p. 50-51].

Bayer claims that, in each of the studies, foreign travel is a confounding variable that must be corrected. This is a spurious argument. There are no data cited by Bayer purporting to show that Campylobacter organisms acquired in a foreign country are any different from Campylobacter organisms acquired in the United States. In addition, symptoms and duration of illness caused by Campylobacter organisms have not been shown in Bayer's Motion through citations to proffered testimony or exhibits, to be any different when acquired overseas than when acquired in the United States. Again, the hearing, including any cross examination permitted, is the proper forum for Bayer to attempt to establish support for these arguments.

Further, the subissue for hearing relevant to this inquiry is "Whether fluoroquinolone-resistant Campylobacter infections in humans have the *potential* to adversely affect human health?" (emphasis added). Clearly, data from other countries or data from this country that include travelers to other countries can assist the trier of fact in determining whether the *potential* to adversely affect human health exists under certain circumstances. And, as noted by Dr. Frank Aarestrup [Aarestrup WDT, G- 1451, p. 2, Lines 14-17], "...evolving resistant

[12] These arguments purport to cover each of the following epidemiological studies: G-589 (Smith), G-394 (Marano), G-780 (cited by Bayer as Neimann), G-1367 (McClellan) and G-1489 (Nelson).

bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem for all countries." As such, these studies aid the Administrative Law Judge and are relevant to this hearing. The epidemiological studies are also reliable and Bayer's Motion with respect to these studies should be denied. Below is a brief summary supporting the admissibility of the five epidemiological studies specifically noted in Bayer's Motion.

A. Smith (G-589). A Daubert type analysis of this exhibit proves that this exhibit is reliable. Dr. Smith's study uses standard epidemiological methodology and analysis to conclude that the duration of diarrhea associated with fluoroquinolone-resistant Campylobacter is longer than that associated with fluoroquinolone-sensitive Campylobacter. The study describes itself as a case-comparison study and was published in a respected peer-reviewed journal (The New England Journal of Medicine). There appears to be widespread acceptance of the methodologies used; over 3 dozen members of Dr. Smith's team presumably agreed the methodology was appropriate (see caption to title of document, G-589). The study was conducted and published long before CVM's decision to propose to withdraw Baytril (date of publication, May 20, 1999), so the study is independent of any litigation and was prepared in the normal course of scientific pursuit. Dr. Smith is a witness in this hearing, and therefore available for cross-examination. Finally, Dr. Smith, as a public health epidemiologist [Smith WDT, page 1, Line 26 through Page 2, Line 15] is exceptionally qualified to perform this kind of research. For the above reasons, the Smith study (G-589) meets a Daubert type review and Bayer's motion to strike the study based on any reliability argument should be denied.

B. Nelson (G-1489). A Daubert type analysis of this exhibit proves that this exhibit is reliable. Nelson's study uses standard epidemiological methodology and analysis to conclude that the duration of diarrhea associated with fluoroquinolone-resistant Campylobacter is longer than that associated with fluoroquinolone-sensitive Campylobacter. There appears to be widespread acceptance of the methodologies used; almost a dozen co-authors presumably agreed the methodology was appropriate, several of which are witnesses and available for cross-examination. The study was conducted independent of any litigation and was prepared in the normal course of scientific pursuit. Finally, the listed authors are highly qualified to perform this kind of research. [WDTs, Angulo G-1452; Kassenborg G-1460; and Smith G-1473]. For the above reasons, the Nelson study (G-1489) meets a Daubert type review and Bayer's motion to strike this study based on any reliability argument should be denied.

C. Neimann (G-780). The cited exhibit number, G-780, is not the Neimann data but rather an abstract from a paper written by McClellan, et al., on the prevalence and consequences of fluoroquinolone-resistant Campylobacter infections. For that reason alone, CVM respectfully requests that Bayer's motion be denied with respect to this study. However, if CVM assumes the study Bayer means to refer to is that contained in Exhibit B-561,[13] this evidence meets the reliability standard of a Daubert type review. This study used a well-accepted epidemiological methodology – a matched

[13] An abstract poster authored by Neimann appears at G-455 of this Docket. If Bayer was referring to this document, CVM notes that this case-control study was done in conjunction with normal research activities and not in anticipation of litigation, co-authored by a number of qualified scientists, three of whom are witnesses on CVM's behalf in this hearing [WDTs Molbak G-1488, Aarestrup G-1451, and Wegener G-1483], and available for cross examination, and the data contained therein should be considered reliable.

case control study. While there is no indication whether this study, which appears in a Ph.D. thesis, was peer-reviewed, the thesis process serves as a type of peer review to help establish the study's reliability. This study was not done in anticipation or preparation of this hearing. All of these factors lead to the conclusion that this document is reliable under a Daubert type evaluation. Moreover, Bayer's complaints about its inability to obtain approval from Dr. Neimann to further analyze his data is not relevant or material to whether the study is admissible under Daubert and should not be considered in this regard.

D. McClellan[14] (G-1367). The McClellan abstract is reliable and should not be stricken from the evidentiary record of this hearing. The mere fact that data are presented in an abstract does not mean they are unreliable. The abstract clearly discloses the methodology used (the same widely accepted methodology as in the other studies described herein), the population studied and the results obtained. Further, the study was conducted by CDC personnel as part of their normal research activities, not in anticipation or preparation of this hearing. And, since other CDC employees are listed as co-authors of this abstract, it is reasonable to believe that each co-author provided a type of peer review for the data presented. For the above reasons, the McClellan abstract meets a Daubert type review and Bayer's motion to strike this study based on any reliability argument should be denied.[15]

E. Marano (G-394). Like the McClellan abstract, this abstract discloses the methodology of the study and identifies the populations studied. The abstract itself is

[14] To avoid confusion, Jennifer McClellan and Jennifer Nelson are the same person. Nelson is the currently-used surname.

comprehensive and includes methodology, results, and conclusions sections. Its authors include several CVM witnesses in this matter, including Dr. Kassenborg, Dr. Smith, and Dr. Angulo, so the study is subject to further edification on cross-examination. The study was conducted as part of CDC's normal research activities, not in anticipation or preparation for this hearing. And, as is the case for the McClellan abstract, it is reasonable to believe that other scientists listed as co-authors have served a peer-review function. For the above reasons, the Marano abstract meets a Daubert type review and Bayer's motion to strike this study based on any reliability argument should be denied.

As shown above, each of these studies criticized by Bayer easily passes a Daubert type reliability review, and Bayer's Motion to Strike these documents, and testimony based on these documents, is unfounded and should be denied.

VII. The Sentinel County Study is Relevant and Reliable

Bayer's arguments with respect to the Sentinel County Study are not persuasive. As for relevance, this study directly relates to the issue of hearing by providing data from a CDC-conducted, 12-month survey (during 1989-1990) on the susceptibility of Campylobacter to several antimicrobials, including ciprofloxacin and nalidixic acid. [Angulo WDT, p.14, lines 1-36]. These data are useful to estimate the prevalence of ciprofloxacin resistance among Campylobacter during that time period.

Bayer claims it is unclear about what constitutes the Sentinel County Study [Bayer's Motion, p. 54]. However, Bayer's confusion should not be heard as a valid reason to strike

[15] CVM notes that data from the CDC case control study mentioned in this Section were used for the analyses by Nelson in G-1489, McClellan (now Nelson) in G- 1367, and Marano in G-394.

testimony or data. Rather, such confusion could have been cleared up during discovery and can be explored on cross-examination.

Bayer also argues that this study is unreliable based on the fact that Bayer has been unable to obtain the protocol questionnaire and key for the Sentinel County Study from CVM and CDC [Bayer's Motion, p. 55]. Whether CDC has produced, or will produce, any documents relating to this study through its internal Freedom of Information Act process does not go to the reliability of the study itself. CVM notes that Bayer's arguments in this section appear to be mooted, in any event, by Bayer's receipt of information on the Sentinel County Study from CDC [Bayer's Motion, page 55, footnote 14].[16]

Likewise, Bayer's argument that discrepancies in numbers discussed in various reports utilizing the data from this study does not mean the data itself are unreliable. Rather, alleged discrepancies can be probed on cross examination, if permitted; several CVM witnesses have knowledge of this study and have testified to this study [i.e., WDTs Angulo, G-1452; and Barrett, G-1453]. And, any discrepancies not cleared up on cross examination can be noted in Bayer's post-hearing brief and these factors can be assessed by the Administrative Law Judge in determining how much weight to place on this study and testimony about this study.

Bayer also argues that the Sentinel County Study is unreliable as a pre-approval baseline of fluoroquinolone resistance in Campylobacter because the *standard method* used at the time to distinguish Campylobacter jejuni/coli from other species tested for nalidixic acid resistance [Bayer's Motion, p. 56]. Bayer argues that a Campylobacter that was resistant to nalidixic acid would have been discarded when it *may* have been a quinolone-resistant Campylobacter jejuni

[16] Bayer's argument on page 57-58 of its Motion, that its lack of access to protocol or procedure prevents any discernment of the representativeness of the samples to the U.S. population, has similarly been mooted by Bayer's receipt of the requested information. To the extent any additional questions remain, these questions can be explored on cross-examination, if permitted.

[Bayer's Motion, p. 56]. There is no support for this speculative argument. Bayer does not present evidence on what speciation method each of the sentinel laboratories actually used. The "standard" method at the time of the study noted by Bayer *may* have been used by all, some, or none of these labs and, without some cited evidence to that effect, Bayer should not be allowed to speculate. If, however, this argument is considered, it is important to take into consideration the reason that this "standard" method was considered standard at the time. As Dr. Barrett testified:

> "[A]lthough resistance to nalidixic acid had appeared in thermophillic campylobacters other than *C. lari* by that time, it was still rare (5% of *C. jejuni* or 3% of the combined *C. jejuni/C.coli*) considering that nalidixic acid had been in clinical use for more than 20 years. I considered resistance to be rare enough in 1988 to continue recommending that nalidixic acid susceptibility continue to be used as a diagnostic criterion. Resistance to fluoroquinolones was even more unusual at that time..." [Barrett WDT, G- 1453 page 3, lines 7-13].

Finally, a Daubert type reliability evaluation concludes that data from this sentinel study are reliable and therefore admissible. The study was conducted by CDC, as part of its regular work, not to further any position in litigation (G-624). In fact, this study was conducted prior to any possible withdrawal proceeding, since it occurred well before Baytril was even approved. Therefore data from, and testimony about or relying on, the Sentinel County Study are reliable and admissible, and Bayer's Motion with respect to this study should be denied.

VIII. Molbak's Testimony is Relevant and Reliable

Bayer compliments the power of Dr. Molbak's testimony with its motion to strike the entire testimony. As shown below, Bayer's Motion is overly broad and entirely inappropriate. A careful reading confirms that Dr. Molbak's testimony covers other relevant topics within the issue for this hearing, and that the testimony Bayer complains about concerning the relatively increased sickness, length of sickness and death for persons suffering from fluoroquinolone-

resistant campylobacteriosis, actually begins on page 16 of Dr. Molbak's testimony. CVM believes that Bayer's Motion with respect to Dr. Molbak's testimony should be denied in its entirety. Dr. Molbak's testimony is relevant to the issues of the hearing.

Bayer also seeks to paint Dr. Molbak's scientific work as "unreliable". [Bayer's Motion, at 59]. Bayer's first three sentences attacking Dr. Molbak's work and testimony are enough to illustrate that Bayer's eagerness to attack this testimony has led it to try to strike off more than it can justify:

Bayer's first sentence states (without a citation): "Molbak's method was to seek to associate adverse health events to a previous *Campylobacter* infection by comparing a cohort of culture-proven *Campylobacter* cases one year after infection to the general population." [Bayer's Motion, at 59]. Bayer's failure to provide a citation prevents even a careful reader from promptly determining which study of Dr. Molbak's [there are 26 within the past four years listed at pages 28 - 30 of G-1468] is being attacked. Probably, Bayer meant to refer to the study described by Dr. Molbak beginning at page 12 of his testimony, at line 42. Dr. Molbak's method was not "to seek to associate...events...to a previous infection" as Bayer claims, but was to determine and quantify the excess mortality and morbidity beyond that attributable to underlying illness. [Molbak WDT, page 13, ¶ 37]. The study did this in a large and well-documented population (the entire population of Denmark) covered by a single national health program that provides treatment to citizens and health-care data to researchers. [Molbak WDT, page 12, ¶ 35].

Bayer's second sentence incorrectly states: "His review was based on administrative billing claims data ...". [Bayer Motion at 59]. But Denmark's public health system is not a claims-based system, and hence there is no registry of "billing claims", and of course, Dr. Molbak did not testify that there were billing claims. [Molbak WDT]. A comparison of Bayer's

statement to the text it cites for the statement would reflect this ... but Bayer provided no cite for this allegation, either.

Bayer's third strike in this first paragraph is that "[t]his approach is considered controversial because of imperfect adjustments for comorbidity, lack of validation, and inappropriate statistical modeling methodology." Again, Bayer's citeless allegation and its choice of the mysterious passive "is considered controversial" leave the careful reader wondering **who** considers "this approach" controversial, and why Bayer was willing to make these charges, but unable to support them.[17] By inviting this unknown critic to make such general aspersions, Bayer sought to land the criticisms without having to withstand the examination of any supporting citation, or the cross examination of the presumably perfect critic. This third sentence provides no support for Bayer's motion.

Bayer does cite [Motion, at 59] a recent review for its contention that one element, a co-morbidity index, of the work Dr. Molbak reported had been "found to be limited in recording the entirety of the old patients' pathologies...", but the terms of that limitation reveal that review was limited to elderly patients, whereas Dr. Molbak's work was based upon the entire Danish population, not an elderly subset. [Molbak WDT, p. 12, ¶ 35]. As one of the grounds for its motion to strike the entire Molbak testimony, Bayer goes on to attack the co-morbidity index as "not perfect" and found a citation to an article that stated that "[f]indings suggest that the Charlson Comorbidity Index **can be improved upon**..." [emphasis added] [Bayer's Motion at 60, lines 16 and 18]. Bayer repeats the charge of imperfection in the center of page 61 of its Motion. The Center is willing to concede that most scientific papers and some in this record are "not perfect" and use indices that "can be improved upon". If that were sufficient basis to strike

an exhibit, let alone an entire testimony, this record would be economically compact, but so empty as to be incapable of supporting any decision.

Bayer continues to attack Dr. Molbak's testimony in the bottom paragraph of page 61 of its Motion, where the sixth in a series of Bayer sentences unsupported by citation announces from the safe platform of a statement attributed to no one: "It is well known that the proportional hazards model can give incorrect and biased results **in the presence of missing data** ..." [emphasis added] . Indeed. The Center urges the Administrative Law Judge to reject this part of a motion to strike, supported as it is by the presence of so many missing citations to this hearing.

Bayer fairly notes [Motion, page 63] that one of Dr. Molbak's attachments to his testimony is a report bearing the statement: "This report is a working paper and should not be cited." Dr. Molbak did not rely on citation to that paper, but testified to the work involved. [Molbak WDT, pages 16-22]. Although it was a working paper, Dr. Molbak included it with his testimony for any fair review, and used a typical pre-publication legend on the first page of the paper to avoid precluding a later publication in a peer-reviewed journal. Over-running its legitimate concern, Bayer goes on to unfairly (and the Center believes Bayer has done so without basis in fact) testify without citation that "Neither the paper, methodology nor data have undergone peer review. The paper has not even been submitted for publication." [Bayer Motion at 63]. No citation or explanation is given of how Bayer could purport to know that this work had never been peer reviewed or could purport to know that it had never been submitted for publication. The Center's belief that these two statements by Bayer are inaccurate is based upon information not yet of record, about a publication that the Center has just (last week) learned is now expected within the month. If the Center's information is correct, it will move the

[17] Perhaps it was because a scientist who identifies himself as one who rejects an epidemiological study "because of imperfect adjustment for comorbidity" might have to acknowledge that "imperfections" are widespread in reality,

publication into evidence, and the record will reflect (and the Administrative Law Judge can determine) whether Bayer's statements had any basis in fact when made, or not. In any event, the "working paper" legend near the bottom of the first page of this report is no reason to strike it or the testimony of one of its authors about what he knows and what he did.

Bayer continues its attack on Dr. Molbak's testimony and on his report "Health Effects Associated with Antimicrobial Drug-Resistance in *Campylobacter* spp." by asserting that the "spp." in the title signals that his study cohort "May Include Non-C. Jejuni Infections Such As Serious C. Fetus Infections". [Bayer Motion at 63]. This speculative last straw that Bayer has grasped to attack this report, is demonstrably without support. Dr. Molbak's cohort for this study is the entire population of Denmark. [Molbak WDT at page 12, ¶ 35, line 39]. And the Campylobacter species that afflict this population have been characterized as 94% *C. jejuni* and 6 % *C. coli*, leaving 0 % support for Bayer's suggestion that *C. fetus* might explain away the health effects found by Dr. Molbak and others to be associated *with Campylobacter jejuni* and *coli* . Nielsen, E.M. *et al.* G-459 at 5. Bayer's reference, cited above, to "infections such as serious *C. fetus* infections" [capitals converted to lower-case letters] should not be taken as any implication that other *Campylobacter* infections are less than serious: Dr. Molbak's testimony estimates 25 deaths from Campylobacter, each year in Denmark. [Molbak WDT at 13, ¶ 40, lines 43-44]. This seriousness is evident in Dr. Molbak's testimony, as he describes the higher (than in matched referents) rates of complications and adverse health effects of *Campylobacter*-infected patients, and higher rates of adverse health effects in patients with fluoroquinolone-resistant *Campylobacter* infections than in those with fluoroquinolone-susceptible *Campylobacter* infections. [Molbak WDT at 20-22].

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and in scientific reports of reality, perhaps in his own work?

Bayer's final lunge at striking Dr. Molbak's testimony is that it is not relevant because it does not restrict itself to poultry-caused *Campylobacter* mortality and morbidity, and because it relates to patients who, after all, are "in *Denmark*" [emphasis in original]. [Bayer Motion at 63]. The Center is unaware of evidence in this record that can provide any support for the suggestion that *Campylobacter* gain or lose virulence by passing though or living on a chicken or a turkey. Bayer's motion certainly provides no support for this contention. Nor does Bayer's motion supply any basis to believe that Danes are any more or less likely to succumb to or to resist *Campylobacter* infections than Americans. Indeed testimony and studies in this record will reflect that *Campylobacter* infections move among countries, with little regard to the language or nationality of the poultry or the humans that carry and suffer from the *Campylobacter* infections. This includes the written direct testimony of Drs. Aarestrup, Endtz, Molbak, Tauxe, and Wegener. Bayer's suggestion years ago that fluoroquinolone-resistant diseases and adverse effects that affect Europeans needn't concern Americans [Tollefson WDT at 13] may have achieved its goal in convincing the Center to approve Baytril for American poultry, but the American experience since then has followed the experience of those European countries that permitted fluoroquinolones in poultry. [WDT of Drs. Aarestrup, Endtz, Molbak, Tauxe, and Tollefson]. Bayer's suggestion that we should ignore the knowledge, data, experience and testimony of people from another continent is non-sensical and without support in the record. It provides no support for striking the testimony of Dr. Molbak.

Dr. Molbak's testimony and his attachments are relevant on their face, and are not shown to be less than completely reliable by any of Bayer's allegations. The data that are the subject of Dr. Molbak's testimony easily pass a Daubert type review. The methodology for his study is a matched cohort study. As explained earlier in section II of this response, Bayer's witness, Dr.

Feldman, attaches portions of what he describes as an authoritative text, which lists cohort studies as having an important place in field investigations [Feldman WDT: Attachment #1, p. 107-108].

Further, the data were not generated in anticipation or preparation of this hearing; and, CVM is now informed that Dr. Molbak's research will be published this month. Because the Bayer Motion to Strike this testimony is a reflection of the power of the testimony to advance the issue of this hearing, and does not support its allegation that the testimony is unreliable, Bayer's Motion should be denied. Bayer may question as to any fair concerns about this testimony to the extent that the Administrative Law Judge permits cross examination on it.

IX. Testimony and Documents Regarding Frequency of Campylobacteriosis are Relevant and Reliable

Bayer's Motion, pages 64 to 68, seeks to strike all testimony and documents that represent that: (1) Campylobacter is the leading cause of bacterial gastroenteritis in the U.S.; and (2) there are 2.4 million cases of campylobacteriosis in the U.S. Bayer also seeks to strike all estimates of adverse impacts calculated using the 2.4 million figure. Although Bayer suggests that these statements are unreliable and irrelevant because they are inaccurate, Bayer's claims of inaccuracy are completely unsubstantiated.

The support Bayer provides for asserting that Campylobacter is not the leading cause of bacterial gastroenteritis is elusive. Bayer claims, "According to CDC Campylobacter is no longer, and has not been for some time the leading cause of bacterial gastroenteritis in the U.S." In fact, Bayer says this twice. Neither time does Bayer provide a source, to the record or elsewhere, that would permit confirming the accuracy of its assertion.

Then, Bayer boldly asserts that the testimony of CVM witness Dr. Angulo is proof that there are not 2.4 million cases of campylobacteriosis in the U.S.[18] According to Bayer, "The testimony of Angulo confirms that the correct estimated annual incidence of Campylobacter infections is 1.4 million cases in 1999" (emphasis added). What Dr. Angulo actually said was:

> In 1999, the CDC estimated the degree of underreporting of Campylobacter to be approximately 38-fold. Using the FoodNet data from 1996-1997, and correcting for this underreporting, it was estimated that Campylobacter causes 2.4 million infections, 13,000 hospitalizations, and 124 deaths a year in the United States. The frequency of foodborne transmission of Campylobacter was estimated to be 80 percent.
>
> The CDC also used FoodNet data in a more recent model to estimate the burden of Campylobacter. This more recent calculation used FoodNet 1999 Campylobacter incidence and a simulation procedure developed by Vose et al. at the United States Food and Drug Administration in a Campylobacter risk assessment. Using these data and that model, it is estimated that Campylobacter infected an estimated 1.4 million persons in 1999.

[Angulo WDT: p. 7, L4 - 14 (citations omitted)].

As can be seen from the quoted passage, Dr. Angulo was presenting two figures based on two different methods of calculation. Nowhere does Dr. Angulo suggest that one figure, method, or calculation is inaccurate. Moreover, both of these figures are presented as estimates.

For the stated reasons, all testimony and documents that represent that Campylobacter is the leading cause of bacterial gastroenteritis in the U.S. or that there are 2.4 million cases of campylobacteriosis in the U.S., as well as all estimates of adverse impacts calculated using the 2.4 million figure, should not be stricken and this part of Bayer's Motion should be denied.

XI. CVM's Testimony and Exhibits Should Remain in the Evidentiary Record of this Hearing

[18]The figure of 2.4 million cases of campylobacteriosis originates from "Food-Related Illness and Death in the United States," by Paul S. Mead, et al. (G-410).

Below is a chart of responses to Bayer's specific requests to strike portions of CVM's witnesses' written direct testimony and exhibits introduced into the evidentiary hearing. For all the reasons set out above, and below, CVM respectfully requests that Bayer's Motion to Strike be denied.

MASTER LIST OF RESPONSES TO BAYER'S MOTION TO STRIKE CVM'S WRITTEN DIRECT TESTIMONY AND EVIDENCE

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Frank Aarestrup (G-1451)	P. 2, L 9-17	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of Center Response.
	P. 2, L 19-46	see response immediately above
	P. 5, L 4-16	see response immediately above
	P. 5, L 18-23	It is relevant that the samples showed that resistance in veterinary microbiological samples arose after the introduction of enrofloxacin for veterinary use. This is true and relevant, whether the samples were taken for diagnostic or academic motivations.
	P. 6, L 8-22	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of Center Response.
	P. 7, L 3-8	see response immediately above
	P. 7, L 14-17 to P. 8, L 1-5	It is not "speculation", but scientifically appropriate association for an expert to note a consistent pattern of linkage between antimicrobial usage and an increase in resistance. The linkage is all the more remarkable when resistance declines after the antimicrobials are discontinued, and the resistance declines

	P. 8, L 20 - From ("Transferable . . .") - 24	It is relevant that a scientist compares previous complacency to new findings, and is appropriately cautious
	P. 9, L 24-26	This is labeled "Conclusion". The foundation is in the supporting text.
	P. 9, L 32	see response immediately above
	P. 9, L 34-35	Bayer concedes the testimony can apply to some countries, but quarrels with its application to the United States. This makes it subject to briefing and may encourage Bayer to request cross examination. It is no reason to strike the testimony.
	P. 9, L 48 to P. 10, L 2	This testimony is all the more relevant, when read in conjunction with Bayer witness testimony about the conditions in which U.S. poultry are typically raised.
	P. 5, L 18-23	It is relevant that the samples showed that resistance in veterinary microbiological samples arose after the introduction of enrofloxacin for veterinary use. This is true and relevant, whether the samples were taken for diagnostic or academic motivations.
	P. 6, L 8-22	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of Center Response.
	P. 7, L 3-8	see response immediately above
	P. 7, L 14-17 to P. 8, L 1-5	It is not "speculation", but scientifically appropriate association for an expert to note a consistent pattern of linkage between antimicrobial usage and an increase in resistance. The linkage is all the more remarkable when resistance declines after the antimicrobials are discontinued, and the resistance declines
	P. 8, L 20 - From ("Transferable . . .") - 24	It is relevant that a scientist compares previous complacency to new findings, and is appropriately cautious
	P. 9, L 24-26	This is labeled "Conclusion". The foundation is in the supporting text.

	P. 9, L 32	see response immediately above
	P. 9, L 34-35	Bayer concedes the testimony can apply to some countries, but quarrels with its application to the United States. This makes it subject to briefing and may encourage Bayer to request cross examination. It is no reason to strike the testimony.
	P. 9, L 48 to P. 10, L 2	This testimony is all the more relevant, when read in conjunction with Bayer witness testimony about the conditions in which U.S. poultry are typically raised.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Frederick Angulo (G-1452)	P. 2, ¶ 5, L 6 – P. 12, ¶ 12, L 34	See Response, Section IV
	P. 17, ¶ 16, L 12 - From ("In some clinical . . . ") – 13 (". . . reported by NARMS")	See Response, Section IV
	Attachment 1, P. 44-73 (G-1486)	See Response, Section IV. Also, this paper is in press, *Clinical Infections Diseases,* [Angulo WDT, at P. 7, Lines 20-23]
	Attachment 2, P. 74-78 (G-1487)	See Response, Section IV
	Attachment 3, P. 79-107 (G-1488)	Bayer's references to Section IV of its Motion as a reason to strike Angulo's Attachment 3 (G-1488) is spurious. Bayer's Motion, Section IV, does not even address the case-control study at Attachment 3. Bayer's other reason to strike this attachment, i.e., that it is not yet published, is insufficient [see Response, Section VI]
	Attachment 4, P. 108-131 (G-1489)	Bayer's references to Section IV of its Motion as a reason to strike Angulo's Attachment 4 (G-1489) is spurious. Bayer's Motion, Section IV, does not even address the case-control study at Attachment 4. Bayer's other reason to strike this attachment, i.e., that it is not yet published, is insufficient [see Response, Section VI]
	P. 7, ¶ 9, L 10-14	See Response, Sections IV, V
	Attachment 1, pp. 44-73	See Response, Sections IV, V
	P. 15, ¶ 15, L 1 – P. 17, ¶ 15, L 6	See Response, Sections VI, VII
	P. 17, ¶ 16, L 19 - From ("Compared to persons . .) – 22 (". . . treat Campylobacter infections.")	See Response, Section VI

Attachment 3, P. 79-107	Although Bayer's Motion leaves blank its reason to strike, CVM assumes that Bayer intended to indicate that the previously-supplied reason to strike applies also to the testimony listed in this row. Although the assumption has been workable elsewhere, here it is not. Bayer's Motion, Section VI, does not address this testimony
Attachment 4, P. 108-131	See Response, Section VI
Attachment 5, P. 132-141	Bayer's reason for striking this Attachment is nowhere to be found. Perhaps inclusion of this Attachment in Bayer's Motion is in error, as more than one Bayer witness testimony contains the same attachment. [See, e.g., DeGroot (A-200, Attachment 5)]
P. 14, ¶ 14, L 1 – p. 15, ¶ 15, L 10	See Response, Section VII
P. 16, ¶15, L 9-16	See Response, Sections VI, VII
P. 7, ¶ 9, L 5 - From ("using the. . .") – 7 (". . . the United States.")	See Response, Section IX
P. 10, L 22-32 to (". . . of controls.")	Angulo's testimony specifies an adjusted odds ratio that is the same as that contained in Attachment 3, p. 101
P. 13, L 24-30	Angulo's (1) position as Chief of the FoodNet/NARMS Unit of the Foodborne and Diarrheal Diseases Branch at CDC, (2) Ph.D. in Epidemiology, (3) extensive research on the risks and control of foodborne pathogens, put his testimony on the relationship between food handling practices and campylobacteriosis within the scope of his expertise
P. 16, L 28 - From ("More severe . . .") – 37	Angulo's discussion of Salmonella is indeed relevant because it provides a foundation and explanation for his testimony on the possibility that ciprofloxacin-resistant *Campylobacter* may be virulent, causing a longer duration of diarrhea.

	P. 16, L 17-37	The use of the word "might" does not negate the reliability of Angulo's testimony on the results of several studies showing a longer duration of diarrhea in people with ciprofloxacin-resistant *Campylobacter* infections
	P. 10, L 22-32 - to (". . . of controls.")	Repetitive of Bayer's assertion above
	P. 13, L 24-30	Repetitive of Bayer's assertion above
	P. 16, L 28 - From ("More severe . . .") –37	Repetitive of Bayer's assertion above
	P. 16, L 17-37	Repetitive of Bayer's assertion above

WITNESS	TESTIMONY: PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Timothy Barrett (G-1453)	P. 3, ¶ 6, L 13 - From ("In 1939 . . .")- to 20(". . . the 1990s"). P. 4, ¶ 8, L 1-4 (". . . resistant strains.")	See response Section VII
WITNESS	**TESTIMONY: PAGE/LINE**	**REASON TO DENY BAYER'S MOTION TO STRIKE**
Mary Bartholomew (G-1454)	P. 6, L 11-15, 18 - From ("As part . . .") –21	See Response, section IV
	P. 9, L 18-33	See Response, section IV
	P. 11, L 17 - From ("The proportion . . . ")-27	See Response, section IV
	P. 4, ¶ 12, L 8 – P. 20, ¶ 33, L 5	See Response, section V
	P. 8, figure 1, L 1-5	See Response, section IX
	P. 8, L 8-27	Bayer's claim of "better data" cannot be tested, and its motion is therefore unsupported, because the study named is not identified with enough specificity to permit evaluation of the allegation, or even to determine if the Friedman data was published and available when the Campylobacter Resistance Risk Assessment was conducted. Likewise, Bayer's unsupported claim that the Harris and Deming studies are of non-representative subsets of the U.S. population provides no basis for the motion. It is also true that "non-representative subsets of the U.S. population" are entitled to the protection from the hazards of fluoroquinolone-resistant *Campylobacter* in their food, whatever proportion of it is poultry.

	P. 14, L 19-26 - From (". . . could make.")	If the cited figures are really in conflict, the Administrative Law Judge, not Bayer, is the one to determine which figure is the more reliable. The cited passage from Angulo is based on data being cleared in 2002, and it was thus not available for the Campylobacter Resistance Risk Assessment, which was released in 2000, and published in final form in January, 2001. G-953 at 1.
	P. 14, L 43 - From ("Even so . . ") – to 44 (" . . chicken.")	It is not speculation, but observation that runoff or wastewater from poultry raising and processing operations contaminates water. See WDT of Bayer witnesses: Harris at 5, lines 8-16; Patterson at 10, lines 3-17; Woodruff at 13-22.
	P. 14, L 45 - From ("Although . . .") – to 47 (". . . source.")	It is true that the witness did not cite a specific study for the observation that pets may eat food drippings and scraps in a household. The Center believes the Administrative Law Judge may take judicial notice of the fact that pets eat food scraps in the household. If Bayer justifies cross examination on this minor issue, it may inquire of the witness her observational basis for the contention that pets eat household scraps and drippings.
	P. 15, L 19-25 (". . .travel.")	Bayer's mysterious invocation of "CDC data" as a contradiction allows no verification and thus provides no support. For Bayer's contention to be correct, it would have to demonstrate that persons who travel internationally and those who have taken fluoroquinolones as human medicine have not eaten chicken with fluoroquinolone-resistant *Campylobacter* . The testimony properly notes that CVM's treatment of this overlap in exposure is, if anything, favorable to Bayer. The motion is not supported by its own "citation".

	P. 19, L 40 to P. 20, L 5	The foundation for the "Summary" is laid out in the preceding testimony. A risk assessment cannot fairly be faulted for not using the "recent data" that became available after the risk assessment was conducted. See Response, Section V.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
John Besser (G-1455)	P. 10, L 35-42	Besser is a microbiologist and part of the Smith study team. Besser's education, experience, and background qualify him to testify to the reasons for the emergence of fluoroquinolone-resistant campylobacteriosis and the risk posed by the continued use of fluoroquinolones. Moreover, the conclusions he reaches are supported by his testimony on the Smith study [Besser WDT, ¶ 3, ¶ 8 (Lines 18-31)], antibiotic pressure [Besser WDT, ¶ 6.A], and controlling antimicrobial resistance [Besser WDT, ¶ 6.B]

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Hubert Endtz (G-1457)	P. 74-616 (Exhibit G-444)	See Response, section IV, and note that this Exhibit G-444 is a learned treatise which includes work by Bayer witness Newell G-444 pp. 44-61.
	P. 3, L 28-39	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of the Center's Response.
	P. 4, L 27-41	See response immediately above
	P. 8, L 14-20	See response immediately above
	P. 8, L 22-30	See response immediately above
	P. 9, L 34-38	It is not "Speculation" for a witness who is a medical microbiologist to truthfully state his deep concern "about the high level of fluoroquinolone resistance in Campylobacter from poultry and humans" ; and Bayer does not even allege this testimony is not relevant, material, reliable or repetitious. Bayer likewise cites nothing in support of its Motion's contention that fluoroquinolone use in the United States is not large scale. An unsupported motion should be denied. Bayer's vigorous participation in this hearing is a demonstration that it considers it large enough scale to be material; and that is large enough to deny this part of Bayer's motion.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Marja-Liisa Hanninen (G-1458)	P. 2-3, ¶ 3	See Response, Section IV
	P. 5-6, ¶ 8	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of the Centers Response.
	P. 6, ¶ 9	See response immediately above
	P. 2, ¶2 Table 1 & P. 9, ¶ 13 c – Sentence beginning "In countries where fluoroquinolones have never been used."	Bayer's mis-paraphrase of the witness's statement (that fluoroquinolones had "never been **used**") into Bayer's allegation that "Testimony states that fluoroquinolones have never been **approved** in Sweden" [both emphases added] makes a convenient match for the stipulation, but does not accurately paraphrase what the witness said. Bayer is keenly aware of this difference between approval and use, as noted in the general limitation applicable to the very stipulation that Bayer cites: "Any stipulation relating to the registration date of Bayer's ciprofloxacin products or Bayer's enrofloxacin products for poultry contains no representation regarding the dates of sale or use, if any, of Bayer's ciprofloxacin products, or Bayer's enrofloxacin products for poultry in any country, or whether such registrations are currently in effect." Joint Stipulation 50. So the only support offered for this part of Bayer's Motion does not support the motion, and it therefore should be denied, as unsupported.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Heidi Kassenborg (G-1460)	P. 2, ¶, L 11- From ("This organism . . ") – to 12 (" . . annually.") P. 11, ¶ 21, L 7 ("Multiplying . . .") -9	See CVM's Response, Section IX
	P. 10, ¶18, L 1-5 (". . . animals.")	Dr. Kassenborg is qualified to make this conclusion from a review of relevant literature, including G-586, a book chapter by Dr. Kirk Smith in a treatise on Campylobacter edited by Dr. Nachamkin. While her study did not break down risk factors for cases of campylobacteriosis acquired outside the United States, she is qualified to express an opinion on the potential for those cases to be the consequence of fluoroquinolone use in food-producing animals. Joint stipulations as to countries where enrofloxacin is approved for use in poultry and dates of those approvals exist. [Revised Joint Stipulations Nos. 51 through 78] and her testimony discloses the destinations of those 27 foreign travel-associated fluoroquinolone resistant Campylobacter cases [Kassenborg WDT, p. 7, lines 13-17]. Therefore, Dr. Kassenborg's opinion is grounded in the record and is not "pure speculation" as argued by Bayer [Bayer's Motion, Appendix H, p.8].

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Christopher Keeys (G-1461)	Strike entire testimony	Bayer's reasoning for requesting to strike Dr. Keeys testimony in its entirety is faulty for a number of reasons. First, Bayer argues that "there is no testimony to support that his findings are applicable or relevant to the national US population."[Bayer's Motion, Appendix H, p. 8] However, this argument is put to rest by Bayer's own witness, Dr. Kist, who testifies that, "In the US, quinolones are prescribed in approximately 5.2% of all food-borne bacterial diarrhea cases...This is in accordance with data presented in the Direct Testimony of C.A. Keeys (G-1461)..." [Kist WDT, p. 11, Lines 15-19]. Second, Bayer argues that, "the study only mentions Campylobacter species generally, and does not specify whether the patients were treated for *Campylobacter jejuni* or coli. Presumably this would include infections with other Campylobacter, including Campylobacter fetus, as such the testimony does not have relevance to this case which deals with *Campylobacter jejuni* and coli from poultry." [Bayer's Motion, Appendix H, page 8] However, again Bayer's own witness, Dr. Kist, puts this argument in its proper perspective. Dr. Kist states, "In the United States, >99% of reported infections with Campylobacter are with C. jejuni. (Friedman et al., 2000)." [Kist WDT, p. 8, Lines 19-20]. Therefore, Bayer's Motion with respect to Dr. Keeys testimony is without merit and should be denied.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Ken Koziol (G-1462)	Strike entire testimony	Mr. Koziol's testimony is relevant to respond to Bayer's allegations that industry needs Baytril. [See Glisson WDT, p. 6 Lines 9-10 and Hofacre WDT, p. 30, lines 19-20], and that "[W]ithout enrofloxacin, there will be increased production losses... Costs will increase...These costs will be passed on to the consumers." [John Smith WDT, p. 31, Lines 7-9]. Mr. Koziol provides testimony that McDonald's U.S. poultry suppliers (Keystone Foods and Tyson Foods) [Koziol WDT, p. 3, ¶ 7] have not had to use fluoroquinolones in more than three years [Koziol WDT, p. 3, ¶ 7] and that there has been "little impact on the bottom line." [Koziol WDT, p. 3, ¶ 8]

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Stuart Levy (G-1463)	P. 6, ¶ 16, L 16-18	See CVM's Response, Section VI
	P. 7, ¶ 17, L 41-46	See CVM's Response, Section VI
	P. 8, ¶ 19, L 24-25	See CVM's Response, Section VI
	P. 7, L 17-23	Dr. Levy's testimony is relevant to the issue of the potential of fluoroquinolone-resistant Campylobacter to adversely affect human health. Dr. Levy, a physician with over 30 years of studying antimicrobial resistance [Levy WDT, p. 9, Lines 44-45] is highly qualified to provide this testimony. If Bayer wishes to probe the witness about his basis for this testimony, Bayer is free to request permission to cross-examine Dr. Levy. However, the testimony should remain in the evidentiary record and Bayer's Motion should be denied.
	P. 7, L 33-39	Bayer's Motion to Strike this portion of Dr. Levy's testimony based on relevance is overly broad. First, the portion of Dr. Levy's testimony concerning Salmonella is on page 7, lines 35-37, not lines 33-39. Second, these two lines of testimony with respect to Salmonella are useful to put the testimony regarding Campylobacter into context.

	P. 7, L 41-46	Bayer's Motion to Strike this portion of the testimony is not appropriate. The testimony concerns the examination of medical records of patients with Salmonella and Campylobacter and the results of the records review. It is not possible to strike the testimony with respect to Salmonella and still leave testimony relating to Campylobacter. In this case, the Center urges the ALJ to deny Bayer's motion and to decide what weight to put on the testimony at the appropriate time. Again, if Bayer wishes to delve into this study in more detail, it is free to request permission to cross examine Dr. Levy.

	P. 4, L 41 - P. 9, L 19	The FAAIR report was produced by a non-profit organization "dedicated to research and education on antibiotic use and antibiotic resistance." [Levy WDT p. 1, Lines 2-3). This organization convened a scientific advisory committee to "gather evidence and draw conclusions about human health impacts of antimicrobial use in agriculture." [Levy WDT, p. 4, Lines 3-6]. The report was authored by a variety of scientists and was published as a supplement to the Clinical Infectious Diseases, 1 June 2002, Volume 34, Supplement 3. [Levy WDT p. 5, lines 19-20]. The FAAIR report is relevant to issues in this hearing – it covers all aspects of antimicrobial use in animal agriculture, not just non-therapeutic uses. CVM notes that Bayer's Motion fails to direct the ALJ or CVM to the exact part of the report referred to in the Motion. CVM should not be required to comb through the lengthy exhibit to respond to Bayer's statement. Bayer may probe the exhibit's limitations on cross examination if permitted; and, may argue its limitations in Bayer's post hearing brief, with proper record references.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Catherine Logue (G-1464)	P. 8, L 20 - From ("Such high . . .") - 24	Bayer claims that Dr. Logue's study has no discussion of treatment history of flocks processed and therefore this portion of her testimony is speculation without foundation. Bayer also argues that the testimony is not relevant. Dr. Logue's testimony is not mere speculation. Dr. McDermott [McDermott WDT G-1463] testifies that "in the poultry production environment, the multiplication of resistant Campylobacter under fluoroquinolone selection pressure is the major means of the emergence and dissemination of fluoroquinolone-resistant Campylobacter in chickens and turkeys." [McDermott WDT, p. 6, Lines 13-16] That, combined with the testimony of Bayer's witness, Mr. Martin, that: "Agrimetrics surveyed nineteen turkey companies across the country. Only one company said it did not use Baytril" [Martin WDT, p. 16, lines 12-13] provides a basis and foundation in the record for Dr. Logue's testimony.
	P. 8, L 31 - From ("It is my . . .")– P. 9, L 8	See response immediately above

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Pat McDermott (G-1465)	P. 4, ¶ 11, L 44 - P. 5, ¶ 11, L 1(". . . phenotypes (15).")	See CVM's Response, Section IV; Also, Section IV of Bayer's Motion does not call into question the antimicrobial susceptibility testing methods employed by the human part of NARMS. Section IV of Bayer's Motion does not even apply to this portion of Dr. McDermott's testimony, and thus provides no support for this part of Bayer's Motion.
	P. 6, L 27-36	Dr. McDermott's WDT does disclose a basis for his opinion in the evidentiary record – G-1746.
	P. 7, ¶17, L 45 - From ("I believe . . ."), p. 8, ¶ 17, L 2	The record is clear that fluoroquinolones are used to treat gastroenteritis, including Campylobacter [WDTs of Kist p. 11, lines 13-20; Ohl, p. 13, lines 20-38; and, Thielman, p. 3-4, ¶¶6-7] and that cross resistance exists between classes of fluoroquinolones such as enrofloxacin and ciprofloxacin [WDT Weber, p. 8, Lines 5-13], therefore, contrary to Bayer's assertion, there is a basis in the evidentiary record for this portion of Dr. McDermott's testimony.
	Attachment 2, P. 26-39 (G-1492)	The mere fact that the attachment is a presentation, not a published paper does not make the document unreliable. The presentation was delivered at a scientific meeting, not developed to assist in this hearing. The Center urges the ALJ not to strike this presentation and decide what weight to afford it after relevant cross examination.

	Attachment 4, P. 50-51 (G-1494)	Bayer's Motion to strike this attachment Dr. McDermott's testimony is misplaced since Dr. McDermott does not attach this document to his testimony nor base any of his testimony on this abstract. Since Dr. Tauxe did attach this abstract to his testimony [Tauxe WDT, 1475], CVM will address the factual allegations by Bayer and request that the ALJ deny Bayer's Motion for the following reason: The mere fact that data is presented in an abstract does not mean it is unreliable. The abstract describes the study conducted, and discusses the number of cases and results of the study. It also includes a conclusion based on the data collected by the study. The results are presented in a chart that includes confidence rates (confidence intervals). The study was not conducted in anticipation or preparation of this hearing. The study should be kept in the evidentiary record of this hearing and the ALJ should determine what weight it deserves at the proper time.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Kare Molbak (G-1468)	P. 8, ¶ 21, L 1 - P. 9, Table 4, L 9	See CVM's Response, Section IV
	P. 73-109 (Exhibit G-97)	See CVM's Response, Part IV
	P. 110-173 (Exhibit G-98)	See CVM's Response, Part IV
	P. 174-178 (Exhibit G-99)	See CVM's Response, Part IV
	P. 179-354 (Exhibit G-749)	See CVM's Response, Part IV
	P. 12, L 21 - P. 22, L 6 (Exhibit G-1495)	See CVM's Response, Section VIII
	P. 179-354 (Exhibit G-749)	Bayer's "Reason to Strike" this exhibit states only "See Motion: Section VII", which section does not relate to this exhibit. The Motion is therefore unsupported, and should be denied.
	P. 11, L 13 - From ("It is . . .") -15	It is neither speculation nor unreliable for a scientist to note possible explanations for observations, if only to prevent unwarranted assumptions by others. For example, it is helpful to know that "it is conceivable that gun might be loaded", whether the possibility has been fully demonstrated or not. Persons handling guns and data can be more careful, when they know the possibilities.
	P. 11, L 1-50 (includes tables)	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of the Center's Response.
	P. 12, L 1-19	The ability of bacteria to acquire and be selected for resistance is not limited by political borders. See end of Section VIII of the Center's Response. Additionally, the Belgian experience gives relevant hope that when the poultry-contributed fluoroquinolone resistant *Campylobacter* is reduced, the resistant human infections will decline as well.

	P. 16, L 29 - P. 18 (including tables)	This testimony, relating to treatment failures when the human pathogen involved is resistant to the antimicrobial prescribed, is plainly relevant to the issue in this hearing, whether this pathogen (*Campylobacter*) will be amenable to treatment with Bayer's ciprofloxacin, if resistance has been engendered by use of Baytril in poultry. The demonstration of the principle with other pathogens is relevant, whether dispositive or not.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Glenn Morris (G-1469)	P. 6, ¶ 8, L 12 - From ("The most . . .")- to 17 (". . .usefulness.")	See CVM's Response, Section IV
	P. 3, ¶ 4, L 14 - From ("To place . . .")- 23 P. 6, ¶ 8, L 8-9 (". . . in adults")	See CVM's Response, Section IX
	P. 6, ¶8, L 12 - From ("The most . .) – to 17 (". . . usefulness.")	Bayer moves to strike this segment of the testimony as unreliable because Bayer believes the witness did not use the right statistic from the report. The Center urges the ALJ not to strike such testimony, but to consider the concern in any request for cross examination or post-hearing brief.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Irving Nachamkin (G-1470)	P. 2, ¶ 5, L 31-32 (". . United States.")	See CVM's Response, Section IX
	P.3, ¶ 7, L 15-26	See CVM's Response, Section VIII
	P. 6, ¶ 18, L 15-20	See CVM's Response, Section VII
	P. 7, ¶ 21, L4-14	Contrary to Bayer's argument, Dr. Nachamkin's testimony is not unreliable. Dr. Nachamkin is a highly qualified scientist [Nachamkin WDT, p. 1, Line 29 – p. 2, Line 27] who conducted the study on which he bases this portion of his testimony. The study was not conducted to further CVM's position in the hearing, rather, it is a normal research activity conducted independently of this hearing. Dr. Nachamkin's conclusions, [Nachamkin, WDT p. 7, Lines 4-14] are grounded in his earlier testimony [Nachamkin WDT, p. 6, Line 31 through p. 7, Line 2], and, as Dr. Nachamkin discloses, based on other studies in the published literature. As such, this testimony is relevant and reliable. The fact that isolates are not available for those two years does not relate to the reliability of the available data or to conclusions drawn from that data. Bayer is free to ask for permission to cross-examine this witness if it wants to probe this issue further, but its motion to strike should be denied.

	P. 7, ¶ 22, L16-19	This testimony is relevant. It relates to whether enrofloxacin acts as a selection pressure resulting in the emergence and dissemination of fluoroquinolone resistant Campylobacter and whether those fluoroquinolone resistant Campylobacter are transferred to humans and also relates to the potential for fluoroquinolone-resistant Campylobacter to adversely affect human health. The testimony about the situation in other countries is also relevant, as aptly put by Dr. Frank Aarestrup [Aarestrup WDT, p. 2, Lines 14-17], "...evolving resistant bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem in all countries." In its Motion, Bayer has not cited to any data in the evidentiary record purporting to show that Campylobacter organisms acquired in a foreign country are any different from Campylobacter organisms acquired in the Untied States, with respect to symptoms or duration of illness. For all these reasons, Bayer's Motion to Strike this portion of Dr. Nachamkin's testimony should be denied.

	P. 9, ¶ 28, L 27-28	Contrary to Bayer's argument, Dr. Nachamkin's testimony is reliable. Dr. Nachamkin is a highly qualified scientist [Nachamkin WDT, p. 1, Line 29 – p. 2, Line 27] who conducted the study on which he bases this portion of his testimony. The study was not conducted to further CVM's position in the hearing, rather, it is a normal research activity conducted independently of this hearing. Dr. Nachamkin's conclusions, [Nachamkin, WDT p. 7, Lines 4-14] are grounded in his earlier testimony [Nachamkin WDT, p. 6, Line 31 through p. 7, Line 2], and, as Dr. Nachamkin discloses, based on other studies in the published literature. As such, this testimony is relevant and reliable. The fact that isolates are available for those two years does not relate to the reliability of the available data or to conclusions drawn from that data. Bayer is free to ask for permission to cross-examine this witness if it wants to probe this issue further, but its motion to strike should be denied.
WITNESS	**TESTIMONY, PAGE/LINE**	**REASON TO DENY BAYER'S MOTION TO STRIKE**
Clark Nardinelli (G-1471)	P. 7, ¶ 32, L 17 – P. 10, ¶ 42, L 8	See CVM's Response, Section V
	P. 4, ¶ 20, L 30 – P. 7, ¶ 30, L 11	See CVM's Response, Section VI

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Linda Tollefson (G-1478)	P. 2, ¶ 3, L 19 (NARMS . . .")-23	See CVM's Response, Section IV
	P. 5, ¶ 9, L 2 – P. 13, ¶ 32, L 18	See CVM's Response, Section IV
	P. 14, ¶ 36, L 26 – P. 15, ¶ 37, L 2 (". . pathogen, Campylobacter.")	See CVM's Response, Section IV
	P. 19, ¶ 46, L 22 - From ("The Center . . ") – P. 20, ¶ 47, L 5	See CVM's Response, Section IV
	P. 16, ¶ 39, L 1 - From ("To address . .") – P. 17, ¶ 41, L 31	See CVM's Response, Section V
	P. 3, ¶ 6, L 36-38 (". . G-615")	The witness's statement is relevant and supported by the citation. The citation is reliable as described in the Center's Response, Section IX
	P. 12, ¶ 29, Chart identifying 2001 resistance	The preliminary data for 2001, presented in the testimony at page 12, ¶ 29 are reliable, and are the same data relied upon by Dr. Angulo. Dr. Angulo's WDT discusses the 2001 tables and preliminary trend analyses at pages 8 and 9 of his testimony, and the 2001 data is presented in Attachment 2 to his testimony.
	P. 18, ¶ 44, L 34 ("The Center . . .drugs")	Bayer's "Reason to Strike" is not. The testimony reliably states that there are other effective drugs available, and Attachment A to the testimony provides a list of 11 of them.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Kirk Smith (G-1473)	P. 10, ¶ 22, L 31 – P. 11, ¶ 22, L 37	See CVM's Response, Section VI
	P. 20, ¶ 36, L 31- From ("In addition . . .") - to 38 (". . illness.")	See CVM's Response, Section VI
	P. 3, ¶ 4, L 6 - From ("The sample ..")- to 8 (". . Minnesota.")	Bayer's Motion with respect to this portion of Dr. Smith's testimony is unfounded. Bayer gives no basis from the evidentiary record to support its proposition that the sample is not population based. Further, the objection is based on improper testimony from counsel. Dr. Smith's testimony is describing an epidemiological study that he himself conducted and he is the most qualified person to testify about the study. Bayer's improper and unfounded allegations should not be heard with respect to this portion of the testimony and its Motion should be denied.
	P. 15, ¶ 32, L 35 – P. 21, L 5	The testimony about the situation in other countries is relevant to the potential for fluoroquinolone resistant Campylobacter to adversely affect human health. And, as aptly put by Dr. Frank Aarestrup [Aarestrup WDT, p. 2, Lines 14-17], "...evolving resistant bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem in all countries." Further, Bayer has not cited to any basis in the evidentiary record that the geographic location of the Campylobacter and/or the fluoroquinolone affect resistance or symptoms and duration of illness.

	P. 9, ¶18, L 4 ("Of note . .)-10	Bayer's Motion with respect to this portion of Dr. Smith's testimony is overly broad. Smith WDT, p. 9, lines 4-6 present data concerning the MIC values for the isolates that were resistant to Campylobacter and should not have been included in this portion of Bayer's Motion. In any even, the conclusions drawn by Dr. Smith [Smith WDT, p. 9, lines 6-10] are not "speculation" as Bayer argues, but part of a reasonable scientific evaluation by a scientist. Dr. Smith, as lead scientist on this study, and primary author of the study, is entitled to draw conclusions, and testify to such conclusions, based on his own scientific work.

WITNESS	TESTIMONY: PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Robert Tauxe (G-1475)	P. 4, ¶ 11, L 34 - From ("this means . .") - 41	See CVM's Response, Section VI
	P. 18, ¶ 54, L 18 - From ("The longer . .")- 20	See CVM's Response, Section VI
	P. 2, ¶ 5, L 30 ("The national . .")-38	This testimony refers to the data for the **1997** rate of laboratory-confirmed diagnosed *Campylobacter* infections. Bayer's "Reason to Strike" for this portion of the testimony is solely a reference to Bayer's Motion, Section VII, Bayer's attack on the Sentinel County Study, describing prevalence of resistant *Campylobacter* in the United States **in 1989 – 1990.** Because the Reason to Strike does not provide any support for the motion, the motion should be denied.
	P. 1, ¶3, L 42-43 (". . .countries.") P. 2, ¶ 4, L 10 ("Among . . ")-16 P. 3, ¶ 9, L 45-46 P. 4, ¶ 9, L 1-2(". . .infections.") P. 6, ¶ 14, L 10 ("Outbreaks . .")-14 (". . .27.") P. 18, ¶55, L 22-37	See CVM's Response, Section IX

	P. 15, L 38 - P. 16, L 4	Bayer's motion to strike testimony of a CDC expert as irrelevant or not reliable is unsupported by Bayer's "Reason to Strike". Bayer deems other CDC data from uncited works by two CDC authors to be recent and somehow superior, but this motion fails to specify how or why, or identify the specific superior studies. At the most, Bayer's concerns might urge Bayer to request cross examination of a CDC expert to inquire of his choice of whether and which CDC data were the most appropriate. Bayer's motion for this designated passage does not allege any defect in the earlier studies that impairs their relevance and reliability for the purpose for which they were cited here: to show something about the route of bacteriological contamination from chicken preparation to human infection.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Curtis Travis (G-1479)	P. 8, ¶ 27, L 15-18	See CVM's Response; Section V
	P. 8, ¶ 29, L 29 - From ("The CVM model . .") - 32	Bayer did not claim any "Reason to Strike" for this and all subsequent designated sections of Dr. Travis's WDT in Bayer's Appendix H. These unsupported sections of the Motion should therefore be denied. If, Bayer meant to say "ditto" in the Reason to Strike column for these designated portions, indicating that any reason to strike these sections was found in Section V of their Motion, the Center's response to each one is a similar reference to the Center's Response, Section V.
	P. 8, ¶ 30, L 38 - From ("In the deterministic . . .")- to 41 (". . obtained.")	See Response to second designated portion of Travis WDT as above.
	P. 9, ¶ 32, L 17 - From ("Such an approach . .") - 18	See Response to second designated portion of Travis WDT as above.
	P. 9, ¶ 33, L 37 - From ("A deterministic . .") - 40	See Response to second designated portion of Travis WDT as above.
	P. 10, ¶ 37-38, L 36-37 - From (". . interest."), 44 ("I believe . . . approach.")	See Response to second designated portion of Travis WDT as above.
	P. 11, ¶ 38, L 5 ("The CVM . . .") - 13	See Response to second designated portion of Travis WDT as above.
	P. 12, ¶ 42, L 10-11 (". . parameter uncertainties.")	See Response to second designated portion of Travis WDT as above.
	P. 12, ¶ 43, L 24 ("In practice . . .") - 25	See Response to second designated portion of Travis WDT as above.
	P. 12, ¶ 44, L 28-31	See Response to second designated portion of Travis WDT as above.
	P. 12, ¶ 45, L 36 ("The risk …")-38	See Response to second designated portion of Travis WDT as above.
	P. 13, ¶ 46, L 3("and then . .")-4 (". . consumption."), 17-18, 20-21	See Response to second designated portion of Travis WDT as above.
	P. 13, ¶ 48, L 31 – P. 20, ¶ 75, L 5	See Response to second designated portion of Travis WDT as above.
	P. 16, ¶ 62, L 16-18 (". . the model.")	See Response to second designated portion of Travis WDT as above.

	P. 17, ¶ 65, L 5 ("there are . .")-9, 24 (". . . there currently . .")-25 (". . model.")	See Response to second designated portion of Travis WDT as above.
	P. 17, ¶ 67, L 32-33 (". . pathogens")	See Response to second designated portion of Travis WDT as above.
	P. 17, ¶ 68, L 40-45	See Response to second designated portion of Travis WDT as above.
	P. 18, ¶ 69, L 12 ("the Black . .")-14	See Response to second designated portion of Travis WDT as above.
	P. 18, ¶ 72, L 22-33	See Response to second designated portion of Travis WDT as above.
	P. 18, ¶ 73, L 35-39, 41-42, 44-45	See Response to second designated portion of Travis WDT as above.
	P. 19, ¶ 74, L 1-2	See Response to second designated portion of Travis WDT as above.
	P. 19, ¶ 75, L 18-26	See Response to second designated portion of Travis WDT as above.
	P. 20, ¶ 75, L 1-3	See Response to second designated portion of Travis WDT as above.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
David Vose (G-1480)	P. 5, L 18-23	The testimony is relevant for the reason described in the witnesses previous paragraph – to explain some of the differences between a microbial risk assessment and an antimicrobial resistance risk assessment. The need for a type of risk assessment that the Center can use for a variety of resistance-causing antimicrobials is relevant to the Center's choice of the style of risk assessment, a choice that Bayer seeks to challenge. This testimony is relevant to that choice, and thus this testimony should not be stricken.
	P. 5, L 36-39	Same issue. See response immediately above.
	P. 10, L 15-22	This testimony is relevant and material to the Center's choice of model, a choice that Bayer has argued elsewhere is significant. See Bayer's Motion to Strike, section V. The need for timely decisions, as described in this testimony is a legitimate concern for a health regulator, even if the holder of a currently-marketed drug might prefer a slower approach. Bayer's Reason to Strike for this designated segment of Dr. Vose's testimony also misstates the issue for hearing, which is not "whether there is human health impact from fluoroquinolone use in poultry", but whether Baytril is currently shown to be safe. Neither formulation of the issue justifies this Motion.

WITNESS	TESTIMONY PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Robert Walker (G-1481)	P. 7, L 13 - From ("In my . . .")- to 15 (". . too high.")	Bayer moves to strike this expert opinion as unreliable, calling it "speculation", and following with the word "foundation". The rest of the witness's paragraph makes the foundation for the opinion quite explicit, and demonstrates that this witness is not speculating, but is testifying well within his legitimate field of expertise, on recognized criteria which he uses to form his opinion. The reasons Bayer named in support of this part of its motion do not justify striking the designated testimony.

WITNESS	TESTIMONY: PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
Henrick Wegener (G-1483)	P. 26, ¶ 126, L 1-6	See CVM's Response, Section VI
	P. 26, ¶ 133, L 30-31 (". . .prolonged.")	Bayer's Motion to strike this section includes nothing in the Reason to Strike column. If that means that Bayer offers no reason, then that part of Bayer's motion deserves to be denied, for lack of even alleged support. If Bayer meant to signal "ditto", to copy the next previous line, its only supporting reason to strike this quote of an agreed-upon conclusion of a World Health Organization consultation is a reference to a part of Bayer's Motion that does not mention that consultation. Either alternative leaves this part of Bayer's motion without support, and the motion should be denied.
	P. 26, ¶130, L 14-15	Bayer's only "Reason to Strike" this segment of Dr. Wegener's testimony is "Unreliable – See Motion Section IX", a section of Bayer's Motion that does not mention Dr. Wegener, nor even attempt to impugn the WHO expert consultation quoted in this segment of Dr. Wegener's testimony. This part of the motion is therefore without even a claim of support, and should be denied.

WITNESS	TESTIMONY, PAGE/LINE	REASON TO DENY BAYER'S MOTION TO STRIKE
David White (G-1484)	p. 2, ¶ 3, L 29 ("Nearly . .") -32	See CVM's Response, Section IX
	Although not in exhibit H, Bayer elsewhere objects to p. 3, line 45 – p. 4, line 16.	Bayer objects to this part of Dr. White's testimony by referring back to Section IV of its Motion to Strike [Bayer's Motion, Appendix A, p. 1]. However, Bayer's Motion to Strike, Section IV does not address the retail foods part of the NARMS program, the part of the NARMS program that is the subject of this portion of Dr. White's testimony. Therefore, Bayer's Motion, with respect to this part of Dr. White's testimony is unfounded and should be denied.
WITNESS	**TESTIMONY, PAGE/LINE**	**REASON TO DENY BAYER'S MOTION TO STRIKE**
Christopher Ohl (G-1485)	P. 14, ¶ 42, L 2 – p. 15, ¶ 45, L 12	See CVM's Response, Section VI; In addition, Bayer's Motion is overly broad. Only lines 23-30 deal with the subject listed by Bayer as the reason to strike this testimony, and this part of his testimony is based on Dr. Kirk Smith's study, G-589.
	P. 4, ¶13 , L 41 - From ("Campylobacter . .") - 42. P. 6, ¶ 19, L 6-9 (". . annually.") P. 14, ¶44, L 32-38 (". .jejuni.")	See CVM's Response, Section IX

RESPONSES TO BAYER'S MOTION TO STRIKE EXHIBITS

Government Exhibits:

3 Bayer moves to strike on the basis that this document discusses growth promotion antibiotic use, but the quoted title reveals that it also discusses "related therapeutic agents", and the abstract notes that the paper discusses the association between the occurrence of resistance and the consumption of antibiotics. The expert witness's choice to cite and rely on the article confirms its relevance.

4 Bayer's motion to strike this document is based upon the supposition (unsupported by citation by Bayer in its motion) that the action of bacteria, and particularly the emergence of resistance to fluoroquinolone in food-producing animals, varies, depending on the host animal. Absent a showing by Bayer that bacteria and their pattern of resistance development are different inside pigs than they are inside poultry, the witness's expert determination that the paper is relevant enough to rely upon should prevail, unless overcome by other evidence of record.

29 As a basis for its Motion to Strike, Bayer states that this document is repetitive – it states that G-29 and B-147 are identical. Bayer is not correct. The exhibits are not identical. One is 14 pages; the other is 19 pages. Even if the text were identical, the citation by different witnesses to a given page would be thrown off, by substituting one exhibit number for the other. The Center urges that this exhibit not be stricken, because it is not identical to the one claimed by Bayer to be identical.

52 Bayer moves to strike this document as irrelevant, claiming that it "is an international edition of product information for enrofloxacin. As the conditions for use in the United States are different from those internationally, this document has no relevance to issues at hearing." [Bayer's Motion, Appendix G, pp. 14-15] However, this document is referenced by Dr. McDermott as follows: "An additional problem arises when the dose received by the animals is variable, since the antimicrobial is administered in drinking water to ill (and health) birds. Medication of poultry via the drinking water does not always ensure an adequate dose of active enrofloxacin is taken up by the treated birds (Bayer Product Information manual, Exhibit G-25)." [McDermott WDT, p. 7, lines 4-8] Bayer provides no citations to any evidence in the evidentiary record that birds in other countries drink differently, or different amounts, and gives no citation to any evidence that the conditions for use in the United States are so different than in other countries that this manual would not also apply to conditions in the United States. Therefore, Bayer's Motion, with respect to this document, based on relevance should be denied.

62 Bayer moves to strike this exhibit because pages 3-39 are irrelevant, and discuss growth promotion aspects. Bayer is not correct. G-62 is a two-page exhibit. The motion should be denied.

66 The mere fact that data is presented in a letter to the editor does not make that data unreliable. The data reported was collected in the normal course of work, not for this

hearing, it discloses the cases studied, and the results obtained. The fact the author of the abstract is not a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record.[19] The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

70 Bayer claims that this document is repetitive because it is an older version of a book chapter also found at B-205. But the allegation disproves itself. Bayer admits it is an older version, therefore it is not the same document and is not repetitive.

77 Bayer moves to strike on reliability grounds, because the document is a letter to the editor (of The Lancet), and was not peer-reviewed. The mere fact that data is presented in a letter to the editor does not make that data unreliable. The data reported was collected in the normal course of work, not for this hearing, it discloses the cases studied, and the results obtained. The fact the author of the abstract is not a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record.[20] The Center urges the Administrative Law Judge to allow this document to remain in the evidentiary record and decide what weight to give these data at the proper time.

91 See CVM's Response, Section IV

93 See CVM's Response, Section IV

94 See CVM's Response, Section IV

96 See CVM's Response, Section IV

97 See CVM's Response, Section IV

98 See CVM's Response, Section IV

99 See CVM's Response, Section IV

102 See CVM's Response, Section IV

119 See CVM's Response, Section IV

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[19] Bayer provides no evidence in its Motion that the study or data reported in this letter to the editor or other letters to the editor subject to Bayer's Motion [see, B-412, G-77, G-491, G-530 and G-632] have not themselves been peer reviewed.

[20] Bayer provides no support for its contention that the study or data reported by this abstract, and the other abstracts subject to Bayer's Motion to Strike [i.e., G-141, G-180, G-387, G-399, G-474, G-483, G-499], have not been peer reviewed. Many of the abstracts subject to Bayer's Motion were printed from the "PubMed" website and clearly state the journal in which the study and/or data reported by the abstract were published. Bayer provides no evidence in its Motion that these studies and/or data reported by the abstracts were not, in fact, published in peer reviewed journals. To the contrary, CVM believes that many of these exhibits speak for themselves in this regard.

138 Bayer moves to strike this exhibit for irrelevance because it is an earlier version of Dr. Cox's model. The differences between earlier and later versions of documents can be very relevant to understanding the changes in the author's approach and even to systematic changes. If, after all permitted cross examination, there has been no further reference to the earlier version, that will be time enough to strike the older version. Prior to that, the potential relevance of the document should be preserved by leaving it on the record, available for analysis and citation.

141 The mere fact that data is presented in an abstract does not make that data unreliable. The abstract was done as part of USDA's Agricultural Research Service's normal course of work, not for this hearing, it discloses the population studied and the results obtained. The fact that no author of the abstract is a witness has no effect on the data's reliability. And, while peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

153 Bayer moves to strike this exhibit as repetitive, identical to G-152. But the first two pages reveal that the documents are not identical, and that at least some pages are dark copies and hard to read. Because these two copies are not identical, and because they each may have been cited in different testimonies, the Center urges the Administrative Law Judge not to strike this exhibit.

157 Bayer moves to strike this document on relevance, but concedes that it discusses resistance to antibiotics generally. That discussion demonstrates its relevance. The motion should be denied.

162 Bayer moves to strike this document concerning humans sickened by Campylobacter (and finding a relationship to poultry). Bayer contends that it is not relevant or reliable because its study population (students at the University of Georgia) are a non-representative subset of the U.S. population, and because the study is outdated. Bayer is mistaken, because college students are a representative sub-set of our population. Bayer is free to adduce testimony (and has offered some) on the issue of whether the date of the study reduces its utility now. But the record should not be deprived of the surviving utility of this data, pending the Administrative Law Judge's consideration of the evidence to be offered at oral cross-examination, if any is permitted. The motion should be denied.

180 The mere fact that data is presented in an abstract does not make that data unreliable. The abstract was done in the normal course of work, not for this hearing, it discloses the population studied and the results obtained. The fact that no author of the abstract is a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

205 See CVM's Response, Section IV

206 See CVM's Response, Section IV

207 See CVM's Response, Section IV

268 As with Exhibit 162, Bayer moves to strike this exhibit, alleging that the study population (320,000 members of a health care plan in Washington State) were also not a representative subset of the United States population, and is said to be outdated. As with Exhibit 162, such issues are fair subjects for Bayer to present testimony on, but the exhibits should not be stricken without the Administrative Law Judge's opportunity to evaluate any cross examination about them, whether based on their location or the age of the study.

285 Bayer moves to strike this paper as irrelevant because it addresses another foodborne pathogen, *Salmonella*. But the paper is cited [Tollefson WDT at 3] as an example of the need for the NARMS system, and can assist in establishing the background of the need to understand and control foodborne disease in the United States.

299 Bayer moves to strike a third study because it says the study is of a non-representative subset of the U.S. population and is outdated. This time the allegedly "non-representative subset of the U.S. population" is in Colorado. As with other studies, the record deserves to reflect the studies that are available, and will include Bayer's concerns about them. The study should not be stricken without an opportunity for the Administrative Law Judge to evaluate all the testimony concerning it.

300 Bayer moves to strike this exhibit as repetitious, identical to B-412, but it is a one-page exhibit, and the confusion engendered by striking one of them and leaving references "stranded", pointing to a missing exhibit is greater than the burden of having two one-page versions of the same document. The Center respectfully requests the Administrative Law judge to deny the motion.

320 Bayer is correct that this exhibit is identical to G-315, and the Center does not object to striking either one, so long as a reference to either of them may be fairly be referred to the other.

337 See CVM's Response, Section VI

351 Bayer objects to this document as its discussion of fluoroquinolone resistance is on organisms other than *Campylobacter*. This goes only to the weight accorded to the document, and should not be taken as justifying striking the exhibit.

387 The mere fact that data is presented in an abstract does not make that data unreliable. The abstract was done in the normal course of work, not for this hearing, it discloses the population studied, the methodology used, and the results obtained. The fact that no author of the abstract is a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to

the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

394 See CVM's Response, Section VI

399 The mere fact that data is presented in an abstract does not make that data unreliable. The abstract was done in the normal course of work, not for this hearing, it discloses the population studied and the results obtained. The fact that no author of the abstract is a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

424 Bayer claims that this data is irrelevant to circumstances in the United States. Clearly, data from other countries or data from this country that include travelers to other countries can assist the trier of fact to determine whether the *potential* to adversely affect human health exists under certain circumstances. And, as noted by Dr. Frank Aarestrup [Aarestrup WDT, G- 1451, p. 2, Lines 14-17], "...evolving resistant bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem for all countries." Finally, Bayer has not cited any data in the evidentiary record purporting to show that Campylobacter organisms acquired in a foreign country are any different from Campylobacter organisms acquired in the United States with respect to symptoms or duration of illness. As such, these data aid the Administrative Law Judge and should be considered relevant in this hearing.

455 See CVM's Response, Section VI

474 Bayer objects to this exhibit because it is an abstract. The mere fact that data is presented in an abstract does not make that data unreliable. The fact that no author of the abstract is a witness has no effect on the data's reliability. And, while peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

483 The mere fact that data is presented in an abstract does not make that data unreliable. The abstract was done in the normal course of work, not for this hearing, it discloses the population studied, the methodology used, and the results obtained. The fact that no author of the abstract is a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

491 The mere fact that data is presented in a letter to the editor does not make that data unreliable. The data was collected in the normal course of work, not for this hearing, it discloses the population studied, the methodology used, and the results obtained. The

fact that no author of the letter is a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time. Bayer also claims that this data is irrelevant to circumstances in the United States. Clearly, data from other countries or data from this country that include travelers to other countries can assist the trier of fact to determine whether the *potential* to adversely affect human health exists under certain circumstances. And, as noted by Dr. Frank Aarestrup [Aarestrup WDT, G- 1451, p. 2, Lines 14-17], "...evolving resistant bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem for all countries." Finally, Bayer has not cited any data in the evidentiary record purporting to show that Campylobacter organisms acquired in a foreign country are any different from Campylobacter organisms acquired in the United States with respect to symptoms or duration of illness. As such, these data aid the Administrative Law Judge and should be considered relevant in this hearing.

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589 See CVM's Response, Section VI[21]

592 See CVM's Response, Section VII

624 See CVM's Response, Section VII

632 The mere fact that data is presented in a letter to the editor does not make that data unreliable. The letter was written in the normal course of work, not for this hearing and it discloses data relevant to the issues of the hearing. The fact the author of the abstract is not a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

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[21] Bayer's Motion, Appendix G, p. 14, states for its reason to strike, "See Motion; Section V". However, Section V of Bayer's Motion concerns CVM's Risk Assessment, not the epidemiological studies. Therefore, Bayer's Motion should be denied with respect to G-589 since 1) the motion does not make sense; and, 2) CVM should not be expected to guess what Bayer really meant. If Bayer really intended to move to strike for the reasons set out in Section VI of its Motion, CVM believes the Motion should be denied based on CVM's Response, Section VI.

human health exists under certain circumstances. And, as noted by Dr. Frank Aarestrup [Aarestrup WDT, G- 1451, p. 2, Lines 14-17], "...evolving resistant bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem for all countries." Finally, Bayer has not cited any data in the evidentiary record purporting to show that Campylobacter organisms acquired in a foreign country are any different from Campylobacter organisms acquired in the United States with respect to symptoms or duration of illness. As such, these data aid the Administrative Law Judge and should be considered relevant in this hearing.

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746 The mere fact that data is presented in an abstract does not make that data unreliable. The abstract was done in the normal course of work, not for this hearing, it discloses the population studied, the methodology used, and the results obtained. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. Bayer argues that none of the authors is a witness and therefore the authors are unavailable for cross-examination. While CVM does not believe that an author must be available for cross examination, it points out that Bayer is incorrect: Dr. David White is a listed author on this abstract and is a CVM witness in this hearing [see White WDT, G-1484]. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

749 See CVM's Response, Section IV

771 Bayer objects to this exhibit because it is an abstract. The mere fact that data is presented in an abstract does not make that data unreliable. The fact that no author of the abstract is a witness has no effect on the data's reliability. And, while peer review might add to the

reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

780 See CVM's Response, Section VI

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953 See CVM's Response, Section V

1350 The FAAIR report was produced by a non-profit organization "dedicated to research and education on antibiotic use and antibiotic resistance." [Levy WDT p. 1, Lines 2-3). This organization convened a scientific advisory committee to "gather evidence and draw conclusions about human health impacts of antimicrobial use in agriculture." [Levy WDT, p. 4, Lines 3-6). The report was authored by a variety of scientists and was published as a supplement to the Clinical Infectious Diseases, 1 June 2002, Volume 34, Supplement 3. [Levy WDT p. 5, lines 19-20]. The FAAIR report is relevant to issues in this hearing – it covers all aspects of antimicrobial use in animal agriculture, not just non-therapeutic uses. CVM notes that Bayer's Motion fails to direct the ALJ or CVM to the exact part of the report referred to in the Motion. CVM should not be required to comb through the lengthy exhibit to respond to Bayer's statement. Bayer may probe the exhibit's limitations on cross examination if permitted; and, it may argue its limitations in Bayer's post hearing brief, with proper record references.

1363 See CVM's Response, Section IV

1367 See CVM's Response, Section VI

1486 See Response, Section IV. Also, this paper is in press, *Clinical Infections Diseases,* [Angulo WDT, at P. 7, Lines 20-23]

1487 See CVM's Response, Section IV

1488 Bayer's references to Section IV of its Motion as a reason to strike Angulo's Attachment 3 (G-1488) is spurious. Bayer's Motion, Section IV, does not even address the case-control study at Attachment 3. Bayer's other reason to strike this attachment, i.e., that it is not yet published, is insufficient [see Response, Section VI]

1489 Bayer's references to Section IV of its Motion as a reason to strike Angulo's Attachment 4 (G-1489) is spurious. Bayer's Motion, Section IV, does not even address the case-control study at Attachment 4. Bayer's other reason to strike this attachment, i.e., that it is not yet published, is insufficient [see Response, Section VI]

1492 The mere fact that the attachment is a presentation, not a published paper does not make the document unreliable. The presentation was delivered at a scientific meeting, not developed to assist in this hearing. The ALJ should admit this presentation into evidence and decide what weight to afford it at the proper time.

1494 Bayer's Motion to strike this attachment to Dr. McDermott's testimony is misplaced because Dr. McDermott does not attach this document to his testimony nor base any of his testimony on this abstract. Dr. Tauxe did attach this abstract to his testimony [Tauxe WDT, G-1475] CVM will address the factual allegations by Bayer and requests that the ALJ deny Bayer's Motion for the following reason: The mere fact that data is presented in an abstract does not mean it is unreliable. The abstract describes the study conducted and discusses the number of cases and results of the study. It also includes a conclusion based on the data collected by the study. The results are presented in a chart that includes confidence rates (confidence intervals). The study was not conducted in anticipation or preparation of this hearing. The study should be kept in the evidentiary record of this hearing and the ALJ should determine what weight it deserves at the proper time.

1495 See CVM's Response, Section VIII

1679 See CVM's Response, Section VI

1681 and 1684 Bayer objects to these exhibits because they are abstracts. The mere fact that data is presented in an abstract does not make that data unreliable. The fact that no author of the abstract is a witness has no effect on the data's reliability. And, while peer review might add to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time.

1745 Bayer objects to this document as its discussion of fluoroquinolone resistance is on organisms other than *Campylobacter*. This goes only to the weight accorded to the document, and should not be taken as justifying striking the exhibit.

1746 The mere fact that information is presented in an abstract does not make that data unreliable. The abstract was done in the normal course of work, not for this hearing. The fact the author of the abstract is not a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting

such data to the record. The Administrative Law Judge should allow this abstract to remain in the evidentiary record and decide what weight to give these data at the proper time.

1749 Bayer objects to this paper on the effect on resistance in fecal bacteria of food animals when growth promoting antibiotics were withdrawn from use in food animals, on Bayer's claim that the paper is not relevant because enrofloxacin is not used for growth promotion. But the fact and time course of the reduction in resistance in the bacteria in food animals when antibiotic use is discontinued (as reported in this paper) is relevant to this hearing, so this part of the motion should be denied.

1758 Bayer moves to strike this testimony as irrelevant because it addresses only Salmonella, another foodborne disease. However, this document will assist in understanding the issues of the hearing, and the testimony of Dr. Molbak, Angulo and Aarestrup. Angulo's reference to this exhibit and his discussion of Salmonella is indeed relevant because it provides a foundation and explanation for his testimony on the possibility that ciprofloxacin-resistant *Campylobacter* may be virulent, causing a longer duration of diarrhea.

1761 The exhibit supports Dr. McDermott's testimony that fluoroquinolone-resistant Campylobacter concentrations near or below the MIC are more apt to select for fluoroquinolone-resistant bacteria [McDermott WDT, p. 6, lines 42-43] and is related to the issue of emergence and dissemination of fluoroquinolone-resistant bacteria in general. It also puts Dr. McDermott's testimony about Campylobacter in context, providing information that Campylobacter is not the only bacteria involving this phenomenon.

1766 Bayer moves to strike this paper as irrelevant because it addresses another foodborne pathogen, *Salmonella*. But this New England Journal of Medicine paper is cited by both Dr. Aarestrup and Dr. Molbak (both of whom are authors on the paper) and the paper provides an example of the serious public health effects of an increase in the resistance of bacteria to fluoroquinolones. It is relevant because it shows the harm the Center seeks to avoid, and the need for dedicated public health officials to do something about it.

1784 As a basis for its Motion to Strike, Bayer states that this document is repetitive – it states that G-1784 is identical to G-1743. A quick perusal of the two documents indicates that G-1784 is 137 pages long and G-1743 is 135 pages long. In this respect they are not identical. Because of time constraints, counsel is unable to take the time necessary to see whether 135 of the pages are, in fact identical. Nothing requires that the ALJ strike repetitive documents. That discretion rests with the ALJ under 21 CFR §12.94. In this case, there will be no prejudice to either party or the record to keep both of these documents in the evidentiary record. CVM respectfully requests that Bayer's Motion be denied. If the ALJ does decide to strike this document as repetitive, CVM requests that anytime Exhibit G-1784 appears as a basis for testimony or otherwise in testimony or briefs, that G-1743 be substituted for the stricken exhibit.

1792 Bayer moves to strike this document, claiming that it is unreliable because it is an abstract, not peer reviewed and none of the authors is a witness. But the article's title is "The Burden of Diarrheal Illness in FoodNet, 2000-2001" depicts its relevance and it describes a survey of over 14,000 people in a segment of the population that includes over 25 million people, so it is more representative of the population, as Bayer recognizes is desirable. Dr. Angulo's testimony [Angulo WDT pages 1-10] demonstrates his familiarity with the FoodNet system and his availability can provide additional detail in response to any reliability questions Bayer may have, if cross examination is permitted. This abstract describes a major effort to document aspects of the problems caused by food borne pathogens, including, of course, the diarrrhea caused by *Campylobacter*. Its value in informing the record for this hearing far outweighs the distinction between a published paper and a published abstract.

Bayer Exhibits:

213 As a basis for its Motion to Strike, Bayer states that this document is repetitive – it states that B-213 and B-15 are identical. Nothing requires that the ALJ strike repetitive documents. That discretion rests with the ALJ under 21 CFR §12.94. In this case, there will be no prejudice to either party or the record to keep both of these documents in the evidentiary record. CVM respectfully requests that Bayer's Motion be denied. Further, CVM notes that Bayer submitted both exhibits, B-15 and B-213, and should not now be heard in a motion to strike one as repetitive. If the ALJ does decide to strike this document as repetitive, CVM requests that anytime Exhibit B-213 appears as a basis for testimony or otherwise in testimony or briefs, that B-15 be substituted for the stricken exhibit

252 Dr. Logue cites to this article, co-authored by Dr. Tauxe, a CVM witness, to support her testimony that high incidences of resistance in *Campylobacter* may be attributed to use of antimicrobials in animal husbandry which are selecting for resistant bacterial strains that can be transferred to humans via ingestion of contaminated food and/or water. This exhibit helps put Dr. Logue's testimony into perspective since it indicates that the high levels of resistance in *Campylobacter* have been seen in other bacteria and is not unique, and the document will help the ALJ determine the weight and credibility of Dr. Logue's testimony. Further, Bayer is free to ask permission to cross examine Dr. Logue (as well as a co-author of the B-213, Dr. Tauxe) on this document.

272 This exhibit will assist the ALJ in putting Dr. Logue's testimony about the high incidence of antimicrobial resistant bacteria associated with human illness and changes observed in level and type of resistance found in these organisms into perspective, indicating that antimicrobial resistance is not unique to *Campylobacter*.

362 This exhibit will assist the ALJ in putting Dr. Logue's testimony about the high incidence of antimicrobial resistant bacteria associated with human illness and changes observed in level and type of resistance found in these organisms into perspective, indicating that antimicrobial resistance is not unique to *Campylobacter*.

384 The exhibit will assist the ALJ because it presents information that different meat commodities are not as contaminated with *Campylobacter jejuni* as poultry products are and will put the risk factors of getting a *Campylobacter jejuni* infection from poultry and meat products other than poultry into perspective.

399 This exhibits helps put Dr. Aarestrup's testimony with respect to *Campylobacter* into perspective. The document is relevant to the issues of the hearing in that it talks about the selective pressure of fluoroquinolones on foodborne bacteria.

412 The mere fact that data is presented in a letter to the editor does not make that data unreliable. The data in the letter was collected in the normal course of work, not for this hearing. The letter discloses the population studied, the methodology used, and the results obtained. The fact that no author of the letter is a witness has no effect on the data's reliability. While peer review might lend to the reliability of the data, it is not a prerequisite for admitting such data to the record. The Administrative Law Judge should allow these data to remain in the evidentiary record and decide what weight to give these data at the proper time. Bayer moves to strike a third study because it says the study is of a non-representative subset of the U.S. population and is outdated. This time the allegedly "non-representative subset of the U.S. population" is in Colorado. As with other studies, the record deserves to reflect the studies that are available, and will include Bayer's concerns about them. The study should not be stricken without an opportunity for the Administrative Law Judge to evaluate all the testimony concerning it.

539 Bayer claims that this data is irrelevant to circumstances in the United States. Clearly, data from other countries or data from this country that include travelers to other countries can assist the trier of fact to determine whether the *potential* to adversely affect human health exists under certain circumstances. And, as noted by Dr. Frank Aarestrup [Aarestrup WDT, G- 1451, p. 2, Lines 14-17], "...evolving resistant bacterial population does not respect traditional boundaries between countries. People travel and food of animal origin is traded worldwide. Thus, the development of resistance in any country is an impending problem for all countries." As such, these studies aid the Administrative Law Judge and should be considered relevant in this hearing.

561 See CVM's Response, Section V and VI

589 See CVM's Response, Section VII

762 This document is relevant to the use of ciprofloxacin as an empiric treatment of gastroenteritis

853 Bayer objects to this document as its discussion of fluoroquinolone resistance is on organisms other than *Campylobacter*. This goes only to the weight accorded to the document, and should not be taken as justifying striking the exhibit.

AHI Exhibits:

1 See CVM's Response to Bayer's Motion to Strike Exhibit G-268

20 See CVM's Response to Bayer's Motion to Strike Exhibit G-138

71 See CVM's Response, Section V and VI

Respectfully submitted:

Nadine Steinberg

Robert M. Spiller, Jr.

Claudia Zuckerman

Counsel for the Center for Veterinary Medicine

Enrofloxacin Hearing
Docket No: 00N-1571

CERTIFICATE OF SERVICE

I hereby certify that an original and one copy of the foregoing Center for Veterinary Medicine's Response to Bayer's and AHI's Motions to Strike was hand delivered this 10th day of February, 2003, to:

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane (Room 1061)
Rockville, MD 20852

I also certify that a copy of the Response has been hand delivered and e-mailed, this 10th day of February, 2003, to:

The Office of the Administrative Law Judge
Food and Drug Administration
Room 9-57, HF-3
5600 Fishers Lane
Rockville, MD 20857

I also certify that a copy of this Response was e-mailed and mailed by First Class U.S. mail, this 10th day of February, 2003, to:

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Dated: 2/10/03

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