A comparison of *Salmonella* serotype incidence in FSIS-regulated products and salmonellosis cases

Introduction

On May 14, 2010, FSIS published a Federal Register notice (FSIS, 2010a) that detailed revised performance standards for *Salmonella* species on young chicken (broiler) carcasses measured at post-chill. Public comments on the notice asserted that FSIS did not present evidence that reductions of *Salmonella* incidence on young chicken carcasses at post-chill would offer public health benefits. The comments noted that the Centers for Disease Control and Prevention (CDC) FoodNet data sets did not correlate to FSIS percentages of positive chicken samples. In response to these and other comments, FSIS published the March 21, 2011 Federal Register notice (FSIS, 2011) using CDC outbreak data and case-control studies as evidence for such a relationship. CDC summarized these data in a Memorandum to the Record (CDC, 2011a) that concluded "Poultry products are an important vehicle for human *Salmonella* and *Campylobacter* infections in the United States."

The material presented below continues the discussion by demonstrating a weight-of-evidence[1] approach that includes 1) reasons why it is not appropriate to compare CDC FoodNet salmonellosis rates data directly to trends of *Salmonella* incidence in foods, 2) an analysis of CDC outbreaks from chicken products compared with *Salmonella* contamination rates in young chickens, and 3) an analysis of serotype-specific salmonellosis rates and *Salmonella* serotype incidences in young chickens. In conjunction with the data presented in the CDC Memorandum to the Record, FSIS provides further evidence of the connection between *Salmonella* incidence in young chickens and salmonellosis.

Making the appropriate comparison

To begin, it is important to distinguish the two surveillance datasets available from the CDC to analyze outbreak trends and foodborne illness. First, the CDC Foodborne Disease Outbreak

[1] Weight-of-evidence is a form of plausible reasoning. Support for a hypothesis is provided by observations of phenomena when such observations can be "explained" by the hypothesis. However, it is possible other factors could explain the observations, and that the hypothesis is not an actual (true) explanation. Yet by examining many sets of observations and determining that most support the hypothesis, in the above-described manner, we can say with greater confidence that the hypothesis is true and provides an actual explanation. If we assert the truth of the hypothesis through such a set of examinations, we say that the weight-of-evidence supports the hypothesis. In this case, weight-of-evidence is not a formal statistical approach based on controlled sets of observations within a scientific setting (experiments or surveys designed explicitly to "test" a hypothesis).

Surveillance System (FDOSS) (CDC, 2011b), referred to here as outbreak data, provides information on reported outbreaks (defined as two or more illnesses caused by a common source). Various authorities investigate the source (the pathogen and food product responsible for the outbreak) of the contamination − for about 50 percent of confirmed *Salmonella* outbreaks the investigation does not lead to an identifiable food vehicle. Second, the Foodborne Diseases Active Surveillance Network, referred here as FoodNet (CDC, 2011c), produces annual case rates for several major foodborne pathogens, including *Salmonella*. FoodNet data tracks salmonellosis cases in 10 states, presently covering about 46 million people (approximately one-seventh of the U.S. population). The majority of reported FoodNet salmonellosis cases reflect sporadic cases of *Salmonella* (only about six percent of 2007 reported FoodNet cases were outbreak-related (CDC, 2007)). Importantly, unlike outbreak data, there is no information regarding the food product that might have been associated with the illness. Therefore, FoodNet data are only available as aggregated information from cases due to *all* potential food sources. Thus, it would not be appropriate to infer a relationship between *Salmonella* occurrence in chicken carcasses at post-chill and FoodNet salmonellosis from *all food sources*. That is, salmonellosis rates for all products might not reflect a possible reduction of salmonellosis due to one food product, such as chicken, because there might be at the same time increases in salmonellosis due to other food products. Consequently, the absence of a positive correlation between salmonellosis rates and the incidence of contamination rates on young chicken carcasses over time does not permit dismissing the likelihood that *Salmonella* occurrence in chicken and salmonellosis are causally connected.

Outbreaks and *Salmonella* spp. incidence in young chickens

The CDC outbreak data can include information about the food product suspected to have caused an outbreak but are equivocal regarding relationships between *Salmonella* incidence on a product and salmonellosis rates. Accuracy of product identification and the small number of known outbreaks associated with specific product types create problems in drawing a relationship between human illness and chicken contamination rates.

Figure 1 presents two plots: FSIS estimated year-specific percentages of *Salmonella* positive young chicken Hazard Analysis and Critical Control Points (HACCP) verification samples (FSIS, 2000-2008); and the yearly number of outbreaks associated with chicken products (CDC, 2000-2008) (simple food sources only, for a review see Pires et al., 2009). FSIS adjusted the calculations for the year-

specific HACCP percentages of positive results by volume, within three volume classes (small, medium, large) (FSIS, 2010b; see below for method description). This adjustment, thus, accounted for the differences of class-specific percentage of positive results, where chickens produced within smaller volume class establishments had greater percentage of positive results.

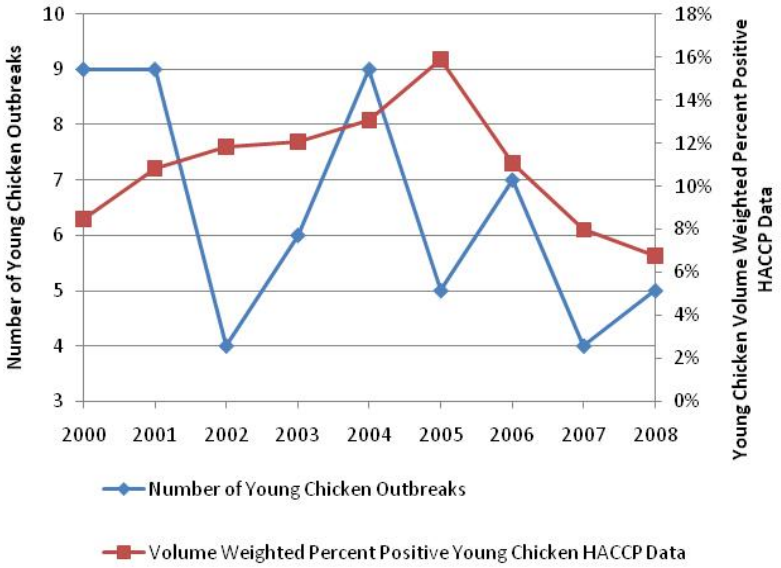

Figure 1. FSIS Volume-Weighted Percent Positive Results from HACCP *Salmonella* Verification Data and the Number of Outbreaks (simple) Associated with Chicken Product from 2000–2008.

Figure 1 shows that the numbers of yearly outbreaks range from 4–9 and seem relatively stable over time. There is an apparent decrease, however, between the years 2005–2008. The decreasing trend in the *Salmonella* contamination on young chicken carcasses covers nearly the same period. The general depicted relationship, however, is not sufficient for asserting that the correlation is positive; the small number of attributed outbreaks per year does not permit an unequivocal statistical relationship to be established.

Salmonellosis cases and *Salmonella* incidence by serotype

A closer review of FoodNet data, at the serotype level, revealed a more definitive relationship. FoodNet often contains serotype information for *Salmonella* associated with human illness. Examining serotypes is a step closer to a direct comparison between *Salmonella* product contamination and salmonellosis attributed to the product because certain *Salmonella* serotypes are mostly associated with particular animal species. For example, FSIS finds *S.* Enteritidis (SE) more

commonly in chicken than in products from other species. FSIS HACCP data indicate that *S*. Enteritidis is found in ground chicken at a rate greater than 100 times that of ground beef[2].

FSIS found that, through examining relationships involving trends of serotype-specific positive results, the weight-of-evidence supports the existence of a relationship between *Salmonella* in a product and illnesses. This relationship requires that for a product, for which a specific serotype is found frequently, a significant positive correlation exists between the serotype-specific FoodNet salmonellosis rate and the serotype-specific percentage of FSIS estimated positive samples for that product (adjusted for volume, as described below). This, however, is not a "deductive" type of conclusion drawn from a "controlled" experiment. Positive correlations for this situation only support the existence of a connection and thus an inferred cause and effect relationship between *Salmonella* contamination on chicken and human illnesses from consumption of contaminated chicken.

Below, FSIS presents an analysis of the top five *Salmonella* serotypes from the 20 most frequently reported *Salmonella* serotypes from human sources identified in the Laboratory-based Enteric Disease Surveillance (LEDS) system by CDC in 2009 (LEDS, 2009). FSIS selected these data because they cover a large percentage of the total confirmed *Salmonella* illnesses, about 60 percent (FoodNet, 2009), provide a manageable amount of data to present, and produce a relatively more accurate method for measuring and comparing trends compared to other serotypes with fewer numbers of cases.

In the following analyses, "FoodNet Relative Rate" is the population-adjusted relative rate versus the 1996–1998 baseline years. Each year is the ratio of the number of confirmed FoodNet cases associated with a serotype, divided by the population-adjusted catchment covered by FoodNet. CDC provided these data to FSIS[3]. CDC adjusted raw data estimates using a negative binomial model to account for increases in number of participating sites (different times of initial participation) and to reduce estimated site-to-site variation in disease incidence (Henao et al., 2010)[4].

[2] Ground products are used for this comparison given that the sampling methodologies can be compared more easily.
[3] Personal communication, CDC February 08, 2011; http://www.cdc.gov/foodnet/factsandfigures/trends.html.
[4] This model assumes that the disease process is similar for those combinations of years and states not observed and are therefore representative of the portion of the U.S. not participating in FoodNet surveillance (Henao et al., 2010).

The "Volume-Weighted (VW) Percent Positive" by serotype and product (FSIS, 2000-2009) for a given year is 100 percent times the volume of contaminated product divided by the total volume for the specified year. We estimate the numerator (volume of contaminated product) by stratifying the establishments that produce the product during the specified year into three strata defined by establishment-specific volumes (for the specified year) and then estimate the volume of contaminated product produced from the establishments within each stratum. Each stratum consists of a set of establishments with production volumes between two specified volume boundaries. For the ith stratum, i = 1, 2 and 3, we designate v_i to represent the sum of the establishment – specific volumes for establishments within the ith stratum. To estimate the volume of contaminated product for the ith stratum, we computed the proportion of *Salmonella* positive samples, p_i, from the FSIS HACCP *Salmonella* Verification program[5] collected from the establishments assigned to the ith stratum during the specified year, and then multiplied p_i by the ith stratum-specific volume. We sum the values $v_i p_i$ over the three strata to estimate the total contaminated volume. We then divided this sum by the total volume of product produced during the year. In the formula, $\hat{p}=100\frac{\sum v_i p_i}{\sum v_i}$ where $\hat{p}$ is the volume-weighted percent positive for the specified year, i is the index for volume stratum, i = 1, 2, 3; v_i is the volume for stratum i; and p_i is the proportion of positive samples in stratum i.

FSIS collects and analyzes HACCP verification samples for eight product classes. For some of these product classes the data are relatively sparse. For example, there were few samples, relatively speaking, for ground chicken (approximately 300 per year compare to approximately 9,000 per year for young chickens), and thus there is large variability of serotype-specific percentages over time. Because there were few *Salmonella* positive results for the steer/heifer carcass class, we combined these data with the cow/bull carcass class. Official collection of young turkey data began in 2006. With the exception of young turkey carcasses, we computed Spearman correlations of the yearly percentages of serotype-specific positive results for HACCP verification samples with the corresponding serotype-specific negative binomial FoodNet-adjusted relative rate for illnesses.

[5] In 2006, FSIS changed its algorithm for determining sampling frequencies of establishments. This could compromise comparison before and after the change. The number of establishments sampled and the number of samples, though, were large before and after the change, and thus we consider these data as "representative" of general trends with respect to *Salmonella* and serotype incidences in FSIS products. Thus, both sets of data are not clearly defined data, in a statistical sense, regarding "representing" well-defined populations. Such data conditions are consistent with a weight-of-evidence approach; in fact necessitate weight-of-evidence approaches based on plausible reasoning.

***S.* Enteritidis** is currently both the most common cause of foodborne salmonellosis (FoodNet, 2009) and the most frequently identified serotype of human health significance among young chickens and ground chicken (FSIS, 2009). Figure 2 compares the CDC estimated *S.* Enteritidis-confirmed FoodNet cases/100,000 with FSIS' adjusted volume-weighted *S.* Enteritidis incidence data for the eight FSIS-regulated product classes. The Spearman correlation of yearly percentages of *S.* Enteritidis in young chickens and *S.* Enteritidis FoodNet illness rate was 0.81 (*p*-value = 0.0049); the correlation was 0.73 (*p*-value = 0.016) for ground chicken; other product classes were not significantly correlated with *S.* Enteritidis human cases. While information for *S.* Enteritidis trends in eggs is missing, the significant positive correlations for young chicken and ground chicken provide support that *S.* Enteritidis incidence in chicken are a contributing source of foodborne salmonellosis due to *S.* Enteritidis exposure.

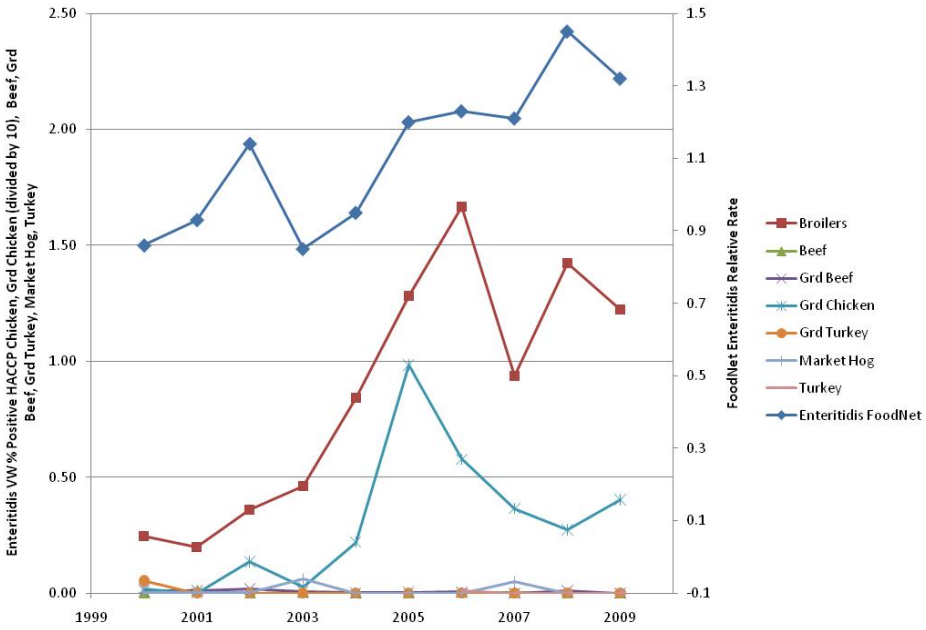

Figure 2[6]. Illness Rates of *S.* Enteritidis in FoodNet and Volume-Weighted Percent Positive Results from HACCP Verification Data from 2000–2009. *Note* the ground chicken data are divided by 10 to fit on the primary y-axis; for example, 2005 reads 0.98 indicating a *Salmonella* incidence of 9.8 percent in ground chicken.

***S.* Typhimurium** is currently the second most common *Salmonella* serotype associated with foodborne illness (FoodNet, 2009) and the third most frequently identified serotype of human health significance among young chickens and ground chicken (FSIS, 2009). This serotype is

[6] Broilers = young chicken carcasses; Turkey = young turkey carcasses; Beef = steer/heifer and cow/bull/bull carcasses; Grd = ground

associated with, and found in, pork, beef, and poultry products. *S.* Typhimurium-associated illnesses have been decreasing since the Agency began its HACCP regulatory approach in the late 1990s. Illness rates associated with *S*. Typhimurium have shown the greatest reduction compared to illness rates associated with single *Salmonella* serotypes among those reported in the most recently completed FoodNet final surveillance report; the report indicates a 52 percent reduction from the combined 1996–1998 baseline (Table 13; FoodNet Surveillance Report, 2007). Unlike the *S.* Enteritidis analysis, the *S.* Typhimurium analysis uses a two-year moving average to smooth out some of the variability in the data (Figure 3). *S.* Typhimurium contamination rates decrease in all the product classes with the possible exception of ground chicken, which can possibly be attributed to variability due to the small numbers of samples analyzed per year. The Spearman correlation of the yearly *S*. Typhimurium illness rates with yearly percentages of *S*. Typhimurium for beef carcasses was 0.66 (*p*-value = 0.038); the correlation for ground turkey was 0.86 (*p*-value = 0.0012); the correlation for market hogs was 0.60 (*p*-value = 0.068); and on the correlation for young chicken carcasses was 0.57 (*p*-value = 0.083). These relationships provide weight-of-evidence support that further reductions of *S*. Typhimurium incidence in meat and poultry products could result in further reduction of *S.* Typhimurium associated FoodNet illnesses.

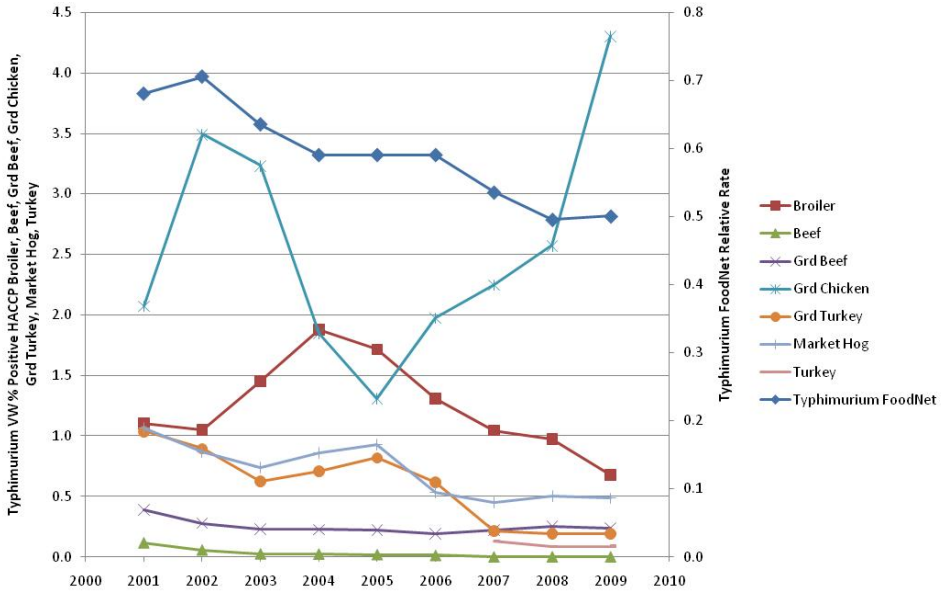

Figure 3. Illness Rates of *S*. Typhimurium[7] in FoodNet and Volume-Weighted Percent Positive Results from HACCP Verification Data from 2000–2009, two-year moving average.

***S.* Newport** is currently the third most common *Salmonella* serotype associated with foodborne illness (FoodNet, 2009). The Agency compared *S*. Newport-confirmed FoodNet cases with volume-

[7] Includes *S.* Typhimurium var 5-.

weighted *S*. Newport incidence data for the eight FSIS-regulated product classes using a two-year moving average (Figure 4). This serotype is rare in young chicken samples while FSIS finds it somewhat frequently in ground turkey (approximately on 1 percent of samples, on average), and to a lesser extent in ground beef (approximately 0.2 percent of samples, on average). Thus, it is unsurprising that the percentages of this serotype in young chickens are not correlated with changes in illness rates (yearly-specific Spearman correlation = 0.017, *p*-value = 0.96). Ground turkey, however, is more frequently contaminated with *S*. Newport and trended better over time with *S*. Newport-associated foodborne illnesses; the correlation was 0.47 (*p*-value = 0.17). FSIS believes that the relationships provide weight-of-evidence support for the premise that decreases in incidence of *Salmonella* serotypes of human health significance in products would have a positive impact on public health.

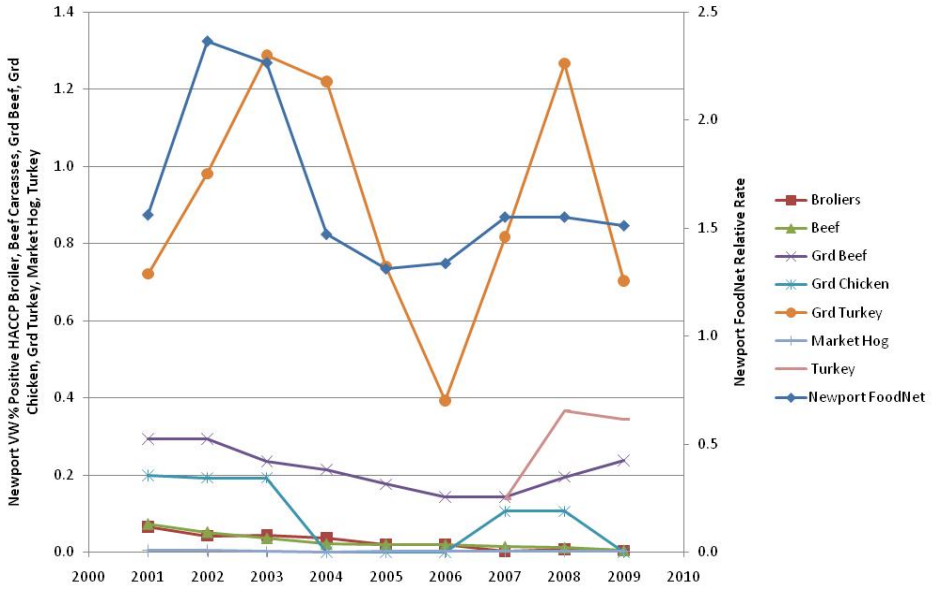

Figure 4. Illness Rates of *S*. Newport in FoodNet and Volume-Weighted Percent Positive Results from HACCP Verification Data from 2000–2009, two-year moving average.

***S.* Javiana** is currently the fourth most common *Salmonella* serotype associated with foodborne illness (FoodNet, 2009). Of more than 500,000 HACCP samples analyzed between 1998 and 2009, FSIS identified only about 30 *S.* Javiana positives from the eight FSIS-regulated product classes, suggesting that *S.* Javiana is not typically associated with FSIS-regulated product classes. Spearman correlation analysis found no significant correlations with the FSIS-regulated products analyzed and human illnesses from *S*. Javiana. However, it appears that this serotype is associated with other foods given the two-fold increase of *S.* Javiana-associated FoodNet illnesses from 2000 to 2009

(Figure 5). This result provides an example of the problem of drawing conclusions regarding the impact of any single food product on illnesses from all found sources.

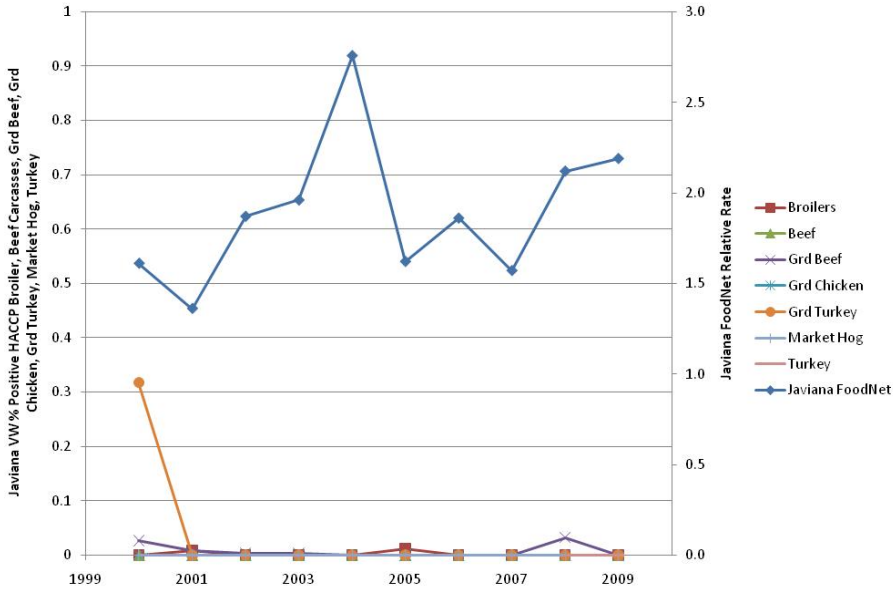

Figure 5. Illness Rates of *S*. Javiana in FoodNet and Volume-Weighted Percent Positive Results from HACCP Verification Data from 2000–2009.

***S.* Heidelberg** is currently the fifth most common *Salmonella* serotype associated with foodborne illness (FoodNet, 2009) and the second most frequently identified *Salmonella* serotype of human health significance found on young chickens and ground chicken (FSIS, 2009). Salmonellosis illness rates associated with *S.* Heidelberg have decreased from this serotype since 2000 (Figure 6). *S*. Heidelberg is found often in poultry products, to a lesser extent in market hogs, and, recently, infrequently in beef products. Figure 6 presents comparisons of *S.* Heidelberg-confirmed FoodNet cases with *S.* Heidelberg incidence data using a two-year moving average. The Spearman correlation of the yearly *S*. Heidelberg illness rates and the yearly percentages of *S.* Heidelberg found on young chickens was 0.82 (*p*-value = 0.004); it was 0.84 for ground turkey (*p*-value = 0.0022); and it was 0.57 (*p*-value =0.083) for market hogs. These relationships provide weight-of-evidence support that decreased *S.* Heidelberg contamination on poultry has been a contributing factor for the reduction of salmonellosis associated with *S.* Heidelberg.

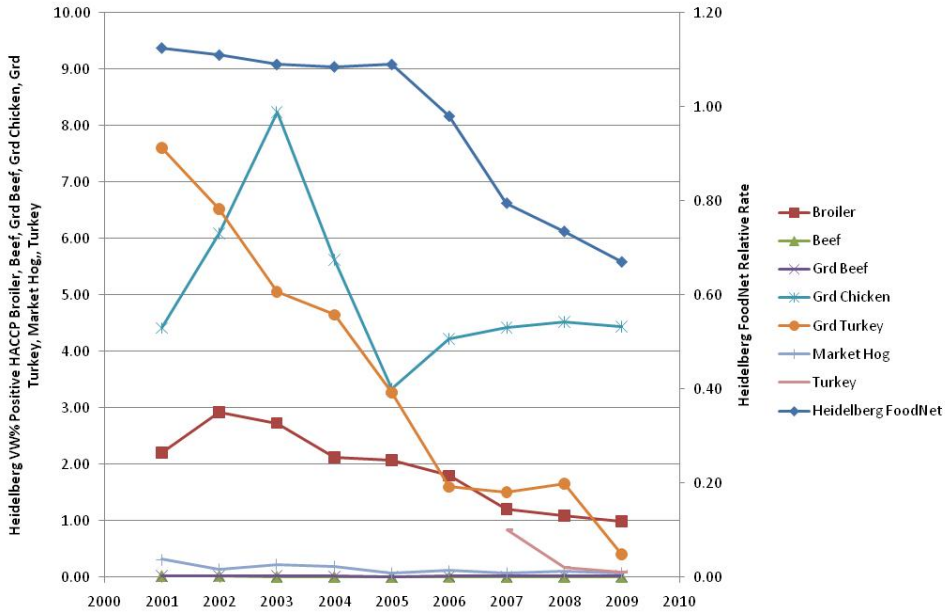

Figure 6. Illness Rates of *S*. Heidelberg in FoodNet and Volume-Weighted Percent Positive Results from HACCP Verification Data from 2000–2009, two-year moving average.

Summary and Conclusion

This analysis stems from comments that claim FSIS did not present data to support the premise that reducing *Salmonella* contamination rates on chicken would reduce human illnesses. For the two serotypes (*S.* Enteritidis and *S*. Heidelberg) that occur commonly in young chickens, the trends in the illness rates attributed to the serotypes and the trends in the percentages of serotype-specific positive results were significantly correlated, with *p*-values less than 0.005. Illness rates associated with *S*. Typhimurium have decreased the most since 2000, which follows the general decrease of *S*. Typhimurium contamination rates for most FSIS-regulated meat and poultry products.

Other product-specific rates rather than that of young chickens may correlate with the illnesses rates; these products' *Salmonella* could be contributing to the positive correlation and not those specifically found on chicken carcasses. Following an examination of serotypes that may or may not be associated with chicken, a pattern appears where, for a serotype associated with certain product types, the percentage of serotype-specific positive results that FSIS found in that product type has a positive correlation with the salmonellosis rate associated with the particular serotype. It is the combination of these patterns, as well as the additional data presented, that provides the weight-of-evidence for the conclusion that reductions of *Salmonella* serotypes associated with illnesses in products lead to reductions of human illnesses in the population.

The five *Salmonella* serotypes discussed represent about 60 percent of the known human *Salmonella* FoodNet cases (FoodNet, 2009); further efforts to reduce the presence of these serotypes, excluding *S.* Javiana, on all FSIS-regulated products should reduce human exposure to disease causing *Salmonella* and thus reduce illnesses. The remaining 40 percent still represent a sizable portion of salmonellosis that is caused by a diverse number of *Salmonella* serotypes (FoodNet Reports, 1998–2009). Many of these serotypes are also found on FSIS-regulated products. FSIS believes that it is entirely reasonable to hold the position that continued efforts to reduce all *Salmonella* serotypes in chicken and turkey carcasses would have a significant impact on reducing or averting illnesses, and thus such efforts are an important part of protecting public health.

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