



United States Department of Agriculture

Food Safety and
Inspection Service

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Laura MacCleery, Director
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1220 L Street N.W.
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FEB 07 2018

Dear Ms. MacCleery:

The Food Safety and Inspection Service (FSIS) has completed its review of the October 1, 2014, petition that David Plunkett and Caroline Smith DeWaal submitted on behalf of the Center for Science in the Public Interest (CSPI). The petition is a refiling of CSPI's petition dated May 25, 2011, requesting that FSIS issue an interpretive rule to declare antibiotic-resistant (ABR) strains of *Salmonella* Hadar, *Salmonella* Heidelberg, *Salmonella* Newport, and *Salmonella* Typhimurium to be adulterants when found in raw ground meat and raw ground poultry. The October 2014 petition includes expanded factual and legal support and requests that FSIS declare these same four ABR *Salmonella* strains to be adulterants in all raw meat and raw poultry products. The October 2014 petition also states that FSIS can consider each of the *Salmonella* strains identified in the petition jointly or individually if the Agency concludes that one or more strains do not merit treatment as an adulterant. The petition incorporates by reference an Appendix that contains information on 1) consumer preparation and cooking practices; 2) *Salmonella* and heat resistance; 3) *Salmonella* and infectious dose; and 4) *Salmonella* and virulence. The petition asserts that if FSIS declares these strains of ABR *Salmonella* to be adulterants in raw meat or raw poultry, the Agency must also take steps to ensure adequate sampling and testing for these pathogens and to remove contaminated raw meat and raw poultry products from the human food supply.

After reconsidering the available data, as well as the expanded legal and factual support included in the petition, we have determined that the available data do not support giving any of the ABR *Salmonella* strains identified in the petition a different status as an adulterant under the Federal Meat Inspection Act (FMIA)(21 U.S.C. 601 *et seq.*) and the Poultry Products Inspection Act (PPIA)(21 U.S.C. 453 *et seq.*) than *Salmonella* strains that are susceptible to antibiotics. The data show that numerous factors, including genetic, environmental, and host-specific factors, interact to make a particular strain pathogenic and virulent. Because of this complexity, we have concluded that antibiotic resistance alone is not an appropriate basis for determining whether a strain should be considered an adulterant. We also disagree with your assertion that ABR *Salmonella* is an "added substance" within the meaning of the

adulteration provisions of the FMIA and PPIA. Therefore, for the reasons discussed below, we are denying your petition without prejudice.

A. ABR *Salmonella* as an “Added Substance”

Summary of Petition:

Adulteration under 21 U.S.C. 601(m)(1) and 453(g)(1)

As noted in your petition, under both the FMIA and the PPIA, a carcass, part thereof, meat, or meat food product, or poultry product is adulterated “if it bears or contains any poisonous or deleterious substance which may render it injurious to health but in case the substance is not an added substance, such article shall not be considered adulterated under this clause if the quantity of such substance in or on such article does not ordinarily render it injurious to health” (21 U.S.C. 601(m)(1) and 453(g)(1)). *Salmonella* is not considered a per se adulterant of raw meat and raw poultry because ordinary cooking and preparation of these products are generally sufficient to destroy the pathogen.¹

In both the original 2011 petition and the resubmitted October 2014 petition, you assert that ABR *Salmonella* has unique characteristics that justify stricter and more uniform treatment than *Salmonella* strains that are susceptible to antibiotics. Specifically, you assert that ABR *Salmonella* is an “added substance” within the meaning of 21 U.S.C. 601(m)(1) and 453(g)(1) because its increasing prevalence is directly attributable to human actions, i.e., the use of antibiotics in animal production. In our response to the 2011 petition, we stated that we had reviewed the published scientific literature and had found studies that indicate that ABR microorganisms may be present in food animals regardless of whether the animals have had exposure to antibiotics. The 2014 petition expands on this and states that although some proportion of ABR microorganisms may be present in food animals regardless of animal exposure to antibiotics, the use of antibiotics distorts the overall population of bacteria, rendering ABR *Salmonella* far more common on meat and poultry products. The petition references *United States v. Anderson Seafoods*,² which held that where some portion of a substance present in a food has been introduced by man, the entirety of that substance present in the food will be treated as an added substance.

¹ See proposed rule “*Pathogen Reduction; Hazard Analysis and Critical Control Point (HACCP) Systems*,” February 3, 1995 (60 FR 6774, 6798-99) and final rule “*Pathogen Reduction; Hazard Analysis and Critical Control Point (HACCP) Systems*,” July 25, 1996 (61 FR 38806, 38835.). See also *Amer. Public Health Ass’n v. Butz*, 511 F.2d 331 (U.S. App. D.C., 1974).

² *United States v. Anderson Seafoods, Inc.*, 622 F. 2d 157 (5th Cir. 1980).

According to the petition, if ABR *Salmonella* is an “added substance,” it can be considered an adulterant in raw meat and poultry if FSIS shows that it “may render” these products “injurious to health.” If a substance is not an added substance, FSIS must show that it would “ordinarily render” a product injurious to health. The petition asserts that the history of outbreaks associated with ABR *Salmonella* and the presence of ABR *Salmonella* in raw meat and raw poultry sold at retail as documented in the petition demonstrate that ABR *Salmonella* “may render” these products injurious to health.

Antibiotic Resistance

In our response to your 2011 petition, we noted that the petition did not define “antibiotic resistance” or specify the number of types of antibiotics that the *Salmonella* strains identified in the petition would need to be resistant to in order to qualify as adulterants. In your 2014 petition, you state that CSPI believes that FSIS has the authority to declare all four strains or any individual strain as an adulterant without regard to a “resistance profile.” Nevertheless, the petition suggests that strains that show resistance to one or more critically or highly important antibiotics, as defined by the World Health Organization (WHO), could provide a reasonable risk management benchmark.³ For the limited purpose of our evaluation, we will not challenge the WHO classification for ABR. In our analysis, we will consider *Salmonella* to be an ABR *Salmonella* strain if it is resistant to one or more critically important or highly important antimicrobial drugs as defined by the WHO. However, please note that in general, FSIS uses the Food and Drug Administration’s (FDA’s) criteria for defining critically important antimicrobial drugs.

FSIS Response:

Added Substance

You state that in denying your 2011 petition, we failed to address the key issue of whether ABR *Salmonella* is an “added substance” within the meaning of 21 U.S.C. 601(m)(1) and 453(g)(1). As noted above, you assert that because ABR *Salmonella* is an “added substance,” it must be held to a different legal standard than other *Salmonella* strains when determining its status as an adulterant. We have considered the expanded legal and factual information included in your petition to support this assertion. Based on our review, we have determined that the available data do not support classifying ABR

³ As noted in the 2014 petition, the WHO classifies an antibiotic as a Critically Important Antimicrobial (CIA) if it is the sole, or one of limited therapy, to treat serious human disease and it is used to treat diseases caused by organisms that may be transmitted or may acquire resistance genes from non-human sources. WHO classifies an antibiotic as a Highly Important Antimicrobial (HIA) if it is the sole, or one of limited therapy, to treat serious human (WHO, WHO List of Critically Important Antimicrobials for Human Medicine (CIA) (2011) at: http://www.who.int/foodsafety/areas_work/antimicrobial-resistance/cia/en/).

Salmonella as a unique “substance” that is separate and distinct from other *Salmonella* strains for purposes of 21 U.S.C. 601(m)(1) and 453(g)(1).

Antibiotic resistance is the ability of a pathogen to resist the effects of an antibiotic. Although antibiotic resistance may affect treatment options for persons infected with *Salmonella*, the ability to cause disease is not unique to ABR *Salmonella*, and available data do not conclusively show that antibiotic resistance directly imparts pathogenicity. In fact, your petition states on page 38 that “the antibiotic-resistant attribute in itself does not heighten *Salmonella*’s pathogenicity.” Thus, it is the pathogen’s presence in a raw meat or raw poultry product and not its resistance to antibiotics that has the potential to render a product “injurious to health.” Many virulent *Salmonella* strains do not exhibit ABR.

We are aware of a study that found *Salmonella* serotypes differ significantly in their pathogenic potential,⁴ and we believe that understanding the mechanisms that make one *Salmonella* serotype more pathogenic than another is important. However, while this study observed differences in severity of disease caused by different *Salmonella* serotypes, it did not collect data on host factors or include information on the resistance patterns of the isolates included in the study. Thus, as discussed below in our response to the Appendix to your petition, additional research is needed to better understand the contribution that antibiotic resistance may play with respect to disease severity.

Although the use of antibiotics in animal production may contribute to the development of the antibiotic resistance attribute, we are not aware of any data to suggest that the potential for raw meat and raw poultry to become contaminated with *Salmonella* differs depending on whether the strain is resistant or susceptible to antibiotics. Infected livestock and poultry carry both ABR and susceptible strains of *Salmonella* in their intestinal tract, and both raw meat and poultry may become contaminated with fecal material containing *Salmonella* during the slaughter operation. We are not aware of any data to suggest that the antibiotic resistant attribute affects this pathway for contamination. We are also not aware of any data to suggest that measures implemented by establishments to prevent or reduce overall *Salmonella* contamination on raw meat or poultry are less effective in preventing or reducing ABR *Salmonella* contamination. In fact, research indicates that intervention strategies aimed at decreasing survival of susceptible *Salmonella* strains on raw meat and raw poultry are also effective against ABR *Salmonella* strains.⁵

⁴ Jones, T. F., L. A. Ingram, P.R. Cieslak, D.J. Vugia, M. Tobin-D'Angelo, S. Hurd, C. Medus, A. Cronquist, and F.J. Angulo. 2008. Salmonellosis outcomes differ substantially by serotype. *J. Infect. Dis.* 198(1): 109-114. doi:10.1086/588823.

⁵ Institute of Food Technologists. 2006. Antimicrobial resistance: implications for the food system. *Comprehensive Rev in Food Sci. and Food Safety.* 5:71-137.

Thus, because it is a pathogen's presence in raw meat or raw poultry and not its resistance to antibiotics that has the potential to render a product "injurious to health," and because the presence of *Salmonella* in raw meat and poultry occurs through, and can be prevented by, the same mechanisms regardless of whether the pathogen is resistant or susceptible to antibiotics, we maintain our initial conclusion that the available data do not support the legal distinction between *Salmonella* and ABR *Salmonella* under the FMIA and PPIA that is suggested in your petition. Thus, we do not believe that ABR *Salmonella* should be considered as a unique "substance" that must be distinguished from other non-ABR *Salmonella* strains for purposes of 21 U.S.C. 601(m)(1) and 453(g)(1).

United States v. Anderson Seafoods

As noted above, you reference *United States v. Anderson Seafoods* to support your assertion that ABR *Salmonella* is an "added substance" under the FMIA and PPIA. As you note, the court in *Anderson Seafoods* held that where some portion of a toxin present in a food has been introduced by man, the entirety of the substance present in the food will be treated as an "added substance." *Anderson Seafoods* involved hazardous levels of mercury in swordfish. In that case, the court found that "if a de minimis amount of the mercury is shown to result from industrial pollution, then all of the metal in the fish is treated as an added substance." You state that the administration of antibiotics in animal production is comparable to the facts in *Anderson Seafoods* in that, although some ABR *Salmonella* may be naturally occurring, the use of antibiotics in farm animals has been shown to increase the prevalence of antibiotic resistant bacteria in meat produced from those animals. You argue that similar to mercury in fish, ABR *Salmonella* qualifies an "added substance" because its increasing prevalence in raw meat and raw poultry is directly attributed to an act of man. However, your analysis fails to address an important difference between the facts in *Anderson Seafoods* and the use of antibiotics in animal production— specifically, the difference between an "added substance" and a genetic attribute.

Unlike mercury, antibiotic resistance is not a substance that can be artificially added to a food. Antibiotic resistance is a genetic trait that exists in some bacteria and is not limited to *Salmonella*. While the administration of antibiotics in animal production may contribute to the survival or development of bacteria with genetic resistance to antibiotics, it does not artificially introduce bacteria in raw meat or raw poultry the way that industrial pollution increased the concentration of mercury in swordfish in *Anderson Seafoods*. As we noted earlier, it is the presence of a pathogen not its resistance to antibiotics that has the potential to render a meat or poultry product "injurious to health." The use of antibiotics may influence the development of a genetic attribute in bacteria, but it does not increase the presence of *Salmonella* or other pathogens in meat or poultry. Furthermore, in *Anderson Seafoods*, the mercury in the fish was added to the environment by man, which contributed to its presence in the swordfish, whereas the presence of *Salmonella* in livestock and poultry is not directly added by man. Therefore,

we disagree that the reasoning in *Anderson Seafoods* can be used to establish that ABR *Salmonella* is an added substance in raw meat and raw poultry.

B. Appendix to the Petition

The 2014 petition also includes an Appendix titled “Factual Basis for Finding ABR *Salmonella* Ordinarily Renders Food Injurious to Health.” The Appendix notes that in FSIS’s denial of CSPI’s 2011 petition, the Agency highlighted certain factors that it considers in determining whether a pathogen should be considered as an adulterant in a raw meat or raw poultry product. In the Appendix, you state that while additional information on these factors as they relate to *Salmonella* “is scientifically important and would add to the body of evidence that ABR *Salmonella* is an adulterant, addressing those factors is not a legal requirement in light of the public health evidence described in the petition that ties ABR *Salmonella* in meat and poultry to human illness.” The Appendix nevertheless includes information and references studies on 1) consumer preparation and cooking practices; 2) *Salmonella* and heat resistance; 3) *Salmonella* and infectious dose; and 4) *Salmonella* and virulence. The petition asserts that this additional information provides further basis for FSIS to grant the petition.

We have reviewed the information included in the Appendix and agree that this information is not critical to your assertion that ABR *Salmonella* is an “added substance” within the meaning of the adulteration provisions of the FMIA and PPIA or that certain ABR *Salmonella* strains should have a different status as an adulterant than non-ABR *Salmonella* strains. As we stated in our response to your initial petition, in 2011, FSIS declared certain Shiga toxin-producing *E. coli* (STEC) to be adulterants in non-intact beef products because the available data show that, like *E. coli* O157:H7, these STECs have a relatively low infectious dose, have been associated with serious illness conditions, such as hemorrhagic colitis and HUS, and that these strains have very similar physiology to the *E. coli* O157:H7 strain so that they can survive what many consumers consider to be proper cooking of ground beef products. We also stated that, based on the available data, *Salmonella* does not appear to present the same issues as STEC, regardless of whether it is resistant or susceptible to antibiotics. We could not find anything in the Appendix to the 2014 petition that would lead us to change this conclusion.

Consumer studies: Your assertion, supported by studies referenced in the Appendix, that consumers do not know the proper methods of food storage, handling, hand washing, cooking, or chilling, does not in itself address fully the concern about whether ABR *Salmonella* in raw product is ordinarily injurious to health. The food preparation and handling studies referenced in the Appendix describe consumer knowledge and practices with respect to refrigerator temperature, hand washing, cross-contamination, and cooking practices, including the use of a thermometer. For example, one survey found that only 3

percent of the participants used a thermometer to check the doneness of chicken,⁶ and another found that 56 percent of participants did not know the recommended refrigerator temperature.⁷ The Agency has, with respect to STEC referred to certain customary cooking practices, e.g., rare or medium rare hamburgers, as an indication of what is an ordinary condition. While most of the studies referenced in the Appendix show that many of the participants were either unaware of or failed to follow safe food handling and preparation practices, they differ from the surveys in which consumers reported cooking ground beef rare, medium rare, or medium, in that the participants in the Appendix studies did not express a specific preference or intent to prepare or consume a meat or poultry product in a manner that is not properly cooked. These studies also did not describe specific characteristics of a meat or poultry product that consumers might mistakenly associate with proper cooking, such as a rare or medium rare hamburger. Many of the studies focused on consumer behavior in preparing chicken, and you note that CSPI did not identify comprehensive studies of consumer practices in their kitchen for all types of meat and poultry. Thus, from the consumer studies and information included in the Appendix, taken together with the other information on *Salmonella* discussed below, we have no basis to conclude that either ABR-*Salmonella* or non-ABR *Salmonella* would render injurious to health what consumers consider to be properly cooked meat or poultry.

Heat resistance: In our response to your 2011 petition, we noted that the available data do not suggest that ABR *Salmonella* is more heat resistant than susceptible *Salmonella* strains. You state that CSPI has not identified studies that show that ABR *Salmonella* strains are more heat resistant than non-ABR *Salmonella* strains, but that heat resistance is not relevant because a study shows that 40 percent of the participants did not cook chicken to a temperature sufficient to kill *Salmonella*.⁸ However, you also reference a separate study that found that while most of the participants did not use a thermometer to evaluate doneness, they still cooked meat and poultry products to a safe internal temperature.⁹ Therefore, based on the studies submitted, the data do not consistently show that consumers undercook product. In addition, you suggest that FSIS consider a study that analyzed *Salmonella* Typhimurium's and certain other pathogens' survivability

⁶ Hoelzl, C., U. Mayerhofer, M. Steininger, W. Brüller, Hofstädter, U. Aldrian. 2013. Observational trial of safe food handling behavior during food preparation using the example of *Campylobacter* spp. *J. Food Prot.* 76(2):482-9. doi:10.4315/0362-028X.JFP-12-231.

⁷ Bruhn, C.M. 2014. Chicken preparation in the home: an observational study. *Food Protection Trend.* 34(5): 318-330. (Bruhn 2014). Accessed at: <http://www.foodprotection.org/files/food-protection-trends/Sep-Oct-14-Bruhn.pdf>

⁸ Bruhn 2014.

⁹ Kendall, P.A., A. Elsebernd, K. Sinclair, M. Schroeder, G. Chen, V. Bergmann, V.N. Hillers, and L.C. Medeiros. 2004. Observation versus self-report: validation of a consumer food behavior questionnaire. *J Food Prot.* 67(11):2578-86.

on chicken.¹⁰ You note that the study concluded that “limited cooking does not necessarily eliminate all bacteria present on the surface of poultry meat.” However, the study does not distinguish ABR *Salmonella* Typhimurium from non-ABR *Salmonella* Typhimurium. Also we did not find anything in the study to suggest that consumers consider “limited cooking” to be a proper or ordinary preparation practice for chicken.

Infectious dose: You state that *Salmonella* infectious dose is dependent on a variety of factors, including host factors in humans, and suggest that for that reason, an evaluation of infectious dose should consider not only factors leading to infection, but also morbidity and mortality. You reference studies involving animals that you believe show that ABR *Salmonella* has a lower dose-response than susceptible *Salmonella*. You also reference studies that you state suggest that the linkage between virulence and antibiotic resistance may also lower infectious dose. You state that, instead of requesting the actual number of *Salmonella* per serving in products responsible for outbreaks, as we did in our first response to your petition, FSIS should rely on other indicators, such as morbidity and mortality factors and antibiotic resistance factors that lower the infective dose for ABR *Salmonella*, as a basis for taking action to reduce the public health risk from ABR *Salmonella*.

While studies referenced in the Appendix suggest animals undergoing treatment with antimicrobial agents may be more prone to infection with resistant organisms due to the void created by suppressed normal flora, this effect is a by-product of altered host susceptibility under abnormal conditions and, thus, is not a direct reflection on the infectivity of ABR *Salmonella* within the general human (or animal) population. The use of antimicrobial drugs selects for resistant *Salmonella* strains disturbing the microbiota of the intestinal tract, placing such individuals at increased risk of certain infections. Individuals taking an antimicrobial agent, for any reason, are at increased risk of becoming infected with pathogens resistant to the antimicrobial agent.¹¹ Thus, we believe that the studies cited in the Appendix do not support inferences about risk beyond a set of circumstances focused on patients being treated for medical conditions who are therefore at increased risk for complications if afflicted with foodborne or any other illness.

Virulence: You note that in our denial of your 2011 petition, we cited limitations to the studies linking virulence to antibiotic resistance in *Salmonella*. You state that our analysis

¹⁰ de Jong, A.E.I., E.D. van Asselt, M.H. Zwietering, M.J. Nauta, R. de Jonge. 2012. Extreme heat resistance of food borne pathogens *Campylobacter jejuni*, *Escherichia coli*, and *Salmonella typhimurium* on chicken breast fillet during cooking. *Int. J. Microbiol.* 2012:1-10. doi:[10.1155/2012/196841](https://doi.org/10.1155/2012/196841).

¹¹ Koningstein M, Simonsen J, Helms M, Molbak K. The interaction between prior antimicrobial drug exposure and resistance in human *Salmonella* infections. *J Antimicrob Chemother* 2010; 65:1819–25. (<http://jac.oxfordjournals.org/content/early/2010/05/26/jac.dkq176>).

of these studies as they apply to ABR *Salmonella* is incomplete. You assert that identification of a specific virulence factor was important in declaring the six STECs as adulterants in raw non-intact beef products because of an absence of strong evidence that those pathogens were causing illnesses and outbreaks. You assert that the same is not true for ABR *Salmonella* because in addition to the outbreak data cited in the petition, numerous studies have found ABR *Salmonella* associated with higher hospitalization rates and poorer health outcomes. It is important to note, however, that highly virulent strains may not exhibit any antimicrobial drug resistance.

Virulence factors for STEC strains are relatively well-characterized and understood. Genes that code for shiga-like toxins have direct bearing on a strain's ability to cause serious illness because the toxins themselves mediate the disease process. Furthermore, it is relatively easy to determine the presence of these toxin-producing genes through routine testing procedures.

In contrast, virulence factors for *Salmonella* are more varied and less identifiable. This is underscored by the fact that both ABR and non-ABR *Salmonella* can cause significant illness. As noted in our response to your 2011 petition, we have found that, although some published articles suggest an association of increased severity of illness with ABR *Salmonella*; these studies are limited in their ability to conclusively determine whether the ABR in itself caused the increased severity.¹² In our response, we also stated that we have not found any published scientific studies that support the proposition that antibiotic resistance and virulence genes always occur together for specific serotypes of *Salmonella*. Our assessment of the available studies has not changed since we issued that response.

One study published in 2014 that was not available when we responded to your first petition analyzed clinical outcomes from FoodNet data and concluded that the results extend evidence that patients infected with some antimicrobial resistance patterns of *Salmonella* have more severe illness outcomes compared with outcomes from infections caused by pan-susceptible *Salmonella* strains. However the study also noted that it had several limitations and stated that “[i]t is possible that some characteristic of patients on which we did not have information (e.g., susceptibility to infection or frequent contact with settings where antimicrobial agents are used, such as hospitals and nursing homes) increased their chances both of acquiring a resistant infection and developing a bloodstream infection, and that the link between resistance and bloodstream infection is not causal.”¹³

¹² See FSIS's July 31, 2014, response to CSPI's 2011 petition, pp 5-6 (<http://www.fsis.usda.gov/wps/wcm/connect/73037007-59d6-4b47-87b7-2748edaa1d3e/FSIS-response-CSPI-073114.pdf?MOD=AJPERES>)

¹³ Krueger, A.L., S.A. Greene, E.J. Barzilay, D. Vugia, D. Hanna, S. Meyer, K. Smith...P.M. Griffin. 2014. Clinical outcomes of nalidixic acid, ceftriaxone, and multidrug-resistant nontyphoidal salmonella infections compared with pansusceptible infections in FoodNet sites, 2006-2008. *Foodborne Pathol. Dis.* 11(5): 335-41. doi:10.1089/fpd.2013.1642.

Another study that was not available when we responded to your first petition integrated resistance and serotype data for nontyphoidal *Salmonellae* infections with case-specific demographic data and some risk factor data, such as international travel.¹⁴ The study found that hospitalization was more likely for patients with clinically important resistant (CIR) *Salmonella* infections than for those with non-CIR *Salmonella* infections. The study defines clinically important resistance as decreased susceptibility to ampicillin, ceftriaxone, ciprofloxacin, gentamicin, or trimethoprim/sulfamethoxazole. The study found that this association was preserved after adjustment for serotype, patient age, patient race, and year. However, the study did not include co-morbidity as a variable in the analysis.

A study by Helms in Denmark that we did not reference in our response to your first petition adjusted for age, sex, and co-morbidity and found a higher risk of invasive illness or death with ABR *S. Typhimurium* compared with susceptible strains.¹⁵ However, the study's authors noted that "it is impossible to determine whether this excess risk of adverse outcomes can be fully explained by reduced efficacy of treatment, because data on antimicrobial drug use were not available in this registry-based study."

A recent paper reviewing National Antimicrobial Resistance Monitoring System (NARMS) surveillance data reported that nontyphoidal *Salmonella* blood isolates were more likely to be resistant to first line treatment agents compared with stool isolates. The article's key point was that this is important for informing clinical decisions regarding appropriate treatment and reducing the burden of antimicrobial resistant nontyphoidal *Salmonella*.¹⁶

C. Other Considerations

The available data show that approximately 80% of human *Salmonella* isolates in the United States are not resistant to any of the tested antimicrobial drugs.¹⁷ This proportion

¹⁴ Barlow, R.S., E.E. DeBess, K.L. Winthrop, J.A. Lapidus, R. Vega, and P.R. Cieslak. 2014. Travel associated antimicrobial drug-resistant nontyphoidal *Salmonellae*, 2004-2009. *Emerg Infect Dis.* 20(4): 603-611. doi: [10.3201/eid2004.131063](https://doi.org/10.3201/eid2004.131063).

¹⁵ Helms M, J Simonsen, K Molbak, 2004. "Quinolone resistance is associated with increased risk of invasive illness or death during Infection with *Salmonella* Serotype Typhimurium." *J Infect Dis* 190 (1 November), 1652-54. doi:10.1086/424570.

¹⁶ Angelo, KM et al. 2016. Antimicrobial Resistance among Nontyphoidal *Salmonella* from Blood in the U.S., 2003-2013. *J Infect Dis*; DOI:10.1093/infdis/jiw415.

¹⁷ NARMS Integrated Report: 2012-2013. The National Antimicrobial Resistance Monitoring System: Enteric Bacteria. 2014.

has not changed in the last 10 years, though resistance in certain serotypes has fluctuated over time. Risks may vary based on serotype, antimicrobial, and food commodity combinations. Research indicates that intervention strategies at processing establishments aimed at decreasing survival of antimicrobial susceptible *Salmonella* strains are also effective against ABR *Salmonella*.^{18,19} A comprehensive review of antimicrobial resistance in the food system by the Institute of Food Technologists concluded that:

*Regulatory targeting of specific antibiotic resistant foodborne pathogens may not be the most successful or cost effective means to reduce overall foodborne illness. A HACCP approach applied throughout the food chain is considered the most effective measure to controlling foodborne pathogens and thereby reducing foodborne illnesses. Most interventions, critical control points to kill or reduce foodborne pathogens, for example, are equally effective in controlling microbes regardless of their resistance to antibiotics. Thus, applying interventions to control foodborne pathogens in general, rather than focusing on antibiotic resistant strains specifically, would have the greatest impact in reducing overall foodborne illnesses.*²⁰

Because the available data indicate that the measures for preventing or reducing foodborne pathogens are equally effective on ABR and susceptible microorganisms, we have concluded that a science-based approach targeted at reducing *Salmonella* in general on raw meat and raw poultry products will result in a more appropriate and effective use of Agency resources compared to a separate and specific focus on ABR *Salmonella*. This is especially important given that the antibiotic resistance traits can be plasmid bound and can move around in *Salmonella* populations, including in diverse serotypes, and can be co-located with other stress tolerance genes and even virulence genes.

FSIS is involved in the active surveillance of antimicrobial resistance in *Salmonella* isolates through the National Antimicrobial Resistance Monitoring System (NARMS). The USDA animal arm of the NARMS has two components—the USDA Pathogen Reduction/Hazard Analysis Critical Control Point (PR/HACCP) sampling and the cecal sampling at slaughter. Antimicrobial susceptibility testing is performed at the FSIS Eastern Laboratory in Athens, Georgia. The NARMS 2012-2013 Integrated Executive Summary reports that about 80% of human *Salmonella* isolates have no resistance detected to any of the tested antimicrobial drugs. Resistance to ceftriaxone, azithromycin,

¹⁸ Hughes, M. K., S. Yanamala, M. San Francisco, G. H. Loneragan, M. F. Miller. 2010. Reduction of multidrug-resistant and drug-susceptible *Salmonella* in ground beef and freshly harvested beef briskets after exposure to commonly used industry antimicrobial interventions. *J Food Prot.* 73:1231-1237.

¹⁹ Capita, R. 2007. Variation in *Salmonella* resistance to poultry chemical decontaminants, based on serotype, phage type, and antibiotic resistance patterns. *J Food Prot.* 70:1835-1843.

²⁰ Institute of Food Technologists. 2006.

and ciprofloxacin—three critically important drugs used to treat human salmonellosis—remains below 3%, although resistance varies by serotype. Additionally, in 2014, there was a decline in the proportion of *Salmonella* isolates from retail chickens that were multi-drug resistant when compared to the 2008-2012 NARMS surveillance data, and full ciprofloxacin resistance has been rare in *Salmonella* isolates from animal and food sources.²¹ We believe that collectively these trends are highly encouraging and protective to U.S. public health.

D. Actions to address illnesses associated with *Salmonella*

In 2014, USDA-FSIS and USDA-Animal and Plant Health Inspection Service (APHIS) signed an MOU to facilitate on-farm investigations in the context of an outbreak associated with FSIS-regulated product.²² Root cause assessments on farm and gathering pre-harvest information will enhance understanding of the source of a foodborne outbreak and help define preventative measures to reduce illnesses due to both non-ABR and ABR *Salmonella*.

When epidemiologic, laboratory, and traceback investigations conducted by local, state, and federal officials provides conclusive evidence identifying the source of a *Salmonella* outbreak, FSIS does consider the implicated product adulterated and conducts recall and other regulatory actions. Since 2009 there have been recalls of raw products due to ABR *Salmonella* Typhimurium (ground beef), ABR *Salmonella* Newport (ground beef), ABR *Salmonella* Hadar (ground turkey), ABR *Salmonella* Heidelberg (ground chicken) and *Salmonella* I 4[5]12:i:-(pork). Outbreak investigative activities require extensive coordination among public health partners; FSIS works closely with the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) and state and local health departments during outbreak investigations in order to collect the information needed for traceback and recall actions. In addition, if FSIS finds a positive *Salmonella* result, it conducts whole genome sequencing (WGS) to better understand the genetic makeup of the pathogen, which would include ABR genes. The Agency also informs the establishment that produced the product of the results.

E. Summary

In summary, FSIS focuses on all the pathogens of concern, including all *Salmonella*, and is committed to its Healthy People 2020 Pathogen Reduction goals. FSIS works closely

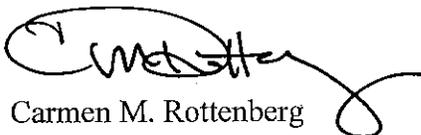
²¹ NARMS Integrated Report: 2014. The National Antimicrobial Resistance Monitoring System: Enteric Bacteria. In press, 2016.

²² MOU dated April 21, 2014 at: <http://www.fsis.usda.gov/wps/wcm/connect/1e6538de-3e99-4bb6-9831-65836899c410/MOU-FSIS-APHIS-One-Health.pdf?MOD=AJPERES>.

with its public health partners and utilizes the best available science to understand the sources of food pathogens and their prevention and control. FSIS is fully committed to utilizing the analytic power and resolution of WGS in its pursuit of pathogen reduction and public health protection, and continues to collaborate with the CDC, FDA and the National Center for Biotechnology Information (NCBI), to further understand the scope and applicability of WGS findings in FSIS's regulatory context. Our goal is to rapidly detect the undesirable traits in pathogens, including virulent strains with or without ABR resistant genes, and prevent and control such pathogens from FSIS regulated foods on an ongoing basis.

For the reasons discussed above, FSIS is denying your October 1, 2014, petition without prejudice. In accordance with our regulations, we have posted your petition on the FSIS Web site. We intend to post this response as well.

Sincerely,

A handwritten signature in black ink, appearing to read 'C. Rottenberg', with a large, sweeping flourish extending to the right.

Carmen M. Rottenberg
Acting Deputy Under Secretary
Office of Food Safety