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Cattle Fever Tick Eradication Program Use of Ivermectin Corn

Final Environmental Assessment, January 2017

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I. Introduction

A. Background

The U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS) is responsible for (1) protecting and improving the health, quality, and marketability of U.S. animals by eliminating animal diseases, and (2) monitoring and promoting animal health and productivity. The Animal Health Protection Act of 2002, as amended, (7 U.S.C. §§ 8301-8317) provides broad authority for APHIS to prevent the introduction into or dissemination within the United States of any pest or disease of livestock (§§ 8303-8305). The Act authorizes prohibition and restriction of the importation, exportation, and interstate movement of animals moving in trade and strays, as well as exportation, inspection, disinfection, seizure, quarantine, destruction and disposal of animals and conveyances (§§ 8303-8308). This includes the ability to "carry out operations and measures to detect, control, or eradicate any pest or disease of livestock" and identifies specific cooperative programs as one way to achieve these actions (§ 8308).

APHIS defines livestock as all farm-raised animals (9 C.F.R. § 71.1). As it relates to tick eradication, Texas defines "animal" as any domestic, free-range, or wild animal capable of hosting or transporting ticks capable of carrying Babesia, including (A) livestock; (B) zebras, bison, and giraffes; and (C) deer, elk, and other cervid species (TEX. AGRIC. CODE § 167.001(1) (see also 4 TEX. ADMIN. CODE § 41.1(2). In Chapter 167, Texas' definition of "livestock" means cattle, horses, mules, jacks, or jennets (TEX. AGRIC. CODE § 167.001(4)).

APHIS established the Cattle Fever Tick Eradication Program (CFTEP) in 1906 as a cooperative State-Federal cattle fever/babesiosis eradication effort, which shared program costs and cooperation between the Federal government, States, local governments, and individual livestock producers. Eradication of two species of cattle fever ticks (*Rhipicephalus* (*Boophilus*) *annulatus* Say, 1821 [Acari: Ixodidae] and *R. microplus* Canestrini, 1888) from the United States occurred by 1943, except in the Permanent Tick Quarantine Zone in South Texas that extends more than 500 miles from Del Rio, Texas to the Gulf of Mexico (figure 1; USDA APHIS, 2015).

To ensure U.S. animal health continues to be unaffected by cattle fever ticks and associated diseases, it is essential to prevent their establishment in this country. With increasing U.S. trade and animal traffic, the risk of cattle fever tick entry and establishment increases. In Central and South America and Africa, cattle diseases and cattle fever ticks are endemic and therefore highly likely to travel with transported animals and associated materials as they enter this country (CFSPH, 2008; Lew-Tabor, 2011; Nakayima et al., 2014). Additionally, there are greater numbers of wildlife hosts such as deer and nilgai antelope. For these reasons, APHIS established and continues to maintain port-of entry inspections and the original Permanent Tick Quarantine Zone.

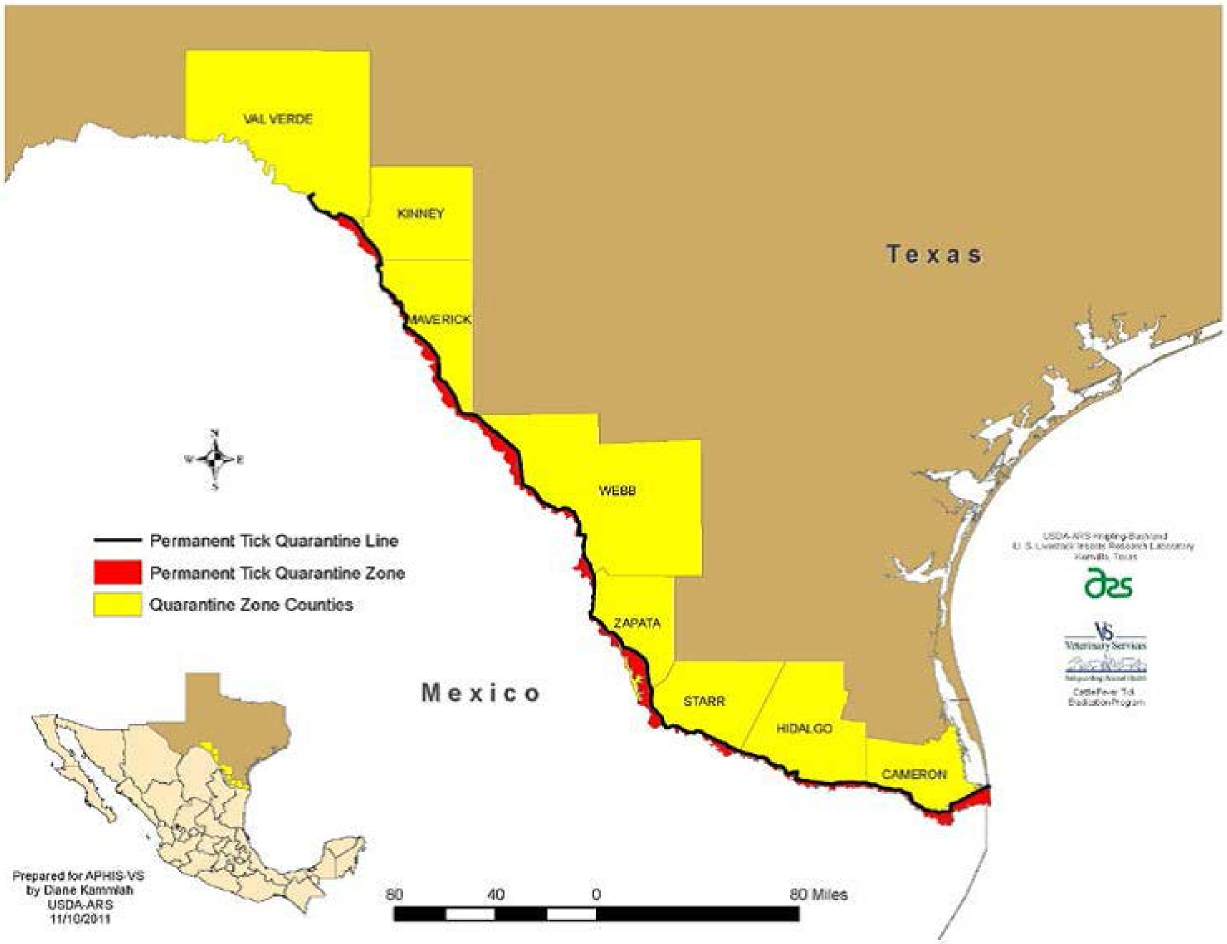

Figure 1. Map of the location of the permanent quarantine line, tick quarantine zone, and quarantine zone counties.

By preventing the establishment of cattle fever ticks in the United States, the CFTEP simultaneously eliminates the disease bovine babesiosis from the U.S. cattle population. Babesiosis is a severe and often fatal disease of livestock caused by protozoan pathogens (*Babesia bovis* V. Babes, 1888 [Piroplasmida: Babesiidae] and *B. bigemina* Smith and Kilbourne, 1893) that is vectored by the two species of cattle ticks. Transmission of this disease requires the presence of these vectors. Babesiosis breaks down the cellular membrane of red blood cells leading to anemia, jaundice, and death. Infected cattle may exhibit neurological disturbances characterized by incoordination, seizures, muscle tremors, hyperexcitability, aggressiveness, blindness, head pressing, and coma. In addition, the two tick species are capable of causing blood loss, significant damage to hides, and an overall decrease in the condition of livestock. There is additional biological information and history of the CFTEP in the "Cattle Fever Tick Eradication Program – Tick Control Barrier, Maverick, Starr, Webb, and Zapata Counties, Texas, Draft Environmental Impact Statement – June 2013", which is incorporated by reference (USDA APHIS, 2013) and referred to as the CFTEP DEIS.

Between October 2011 and September 2014, the incidence of infested premises outside of the Permanent Quarantine Zone remained at 20 or fewer. By December 2014, more than 20 premises in the tick free zone were infested, and that number continues to rise (figure 2). Figure 3 shows the locations of the infestations occurring outside of the Permanent Tick Quarantine Zone and in the Texas Temporary Preventative Quarantine Area. The current increase in infestations combined with a high frequency of infestations occurring outside the Permanent Tick Quarantine Zone suggest current CFTEP inspection and treatment activities may be insufficient to ensure adequate protection of the U.S. livestock industry in the future.

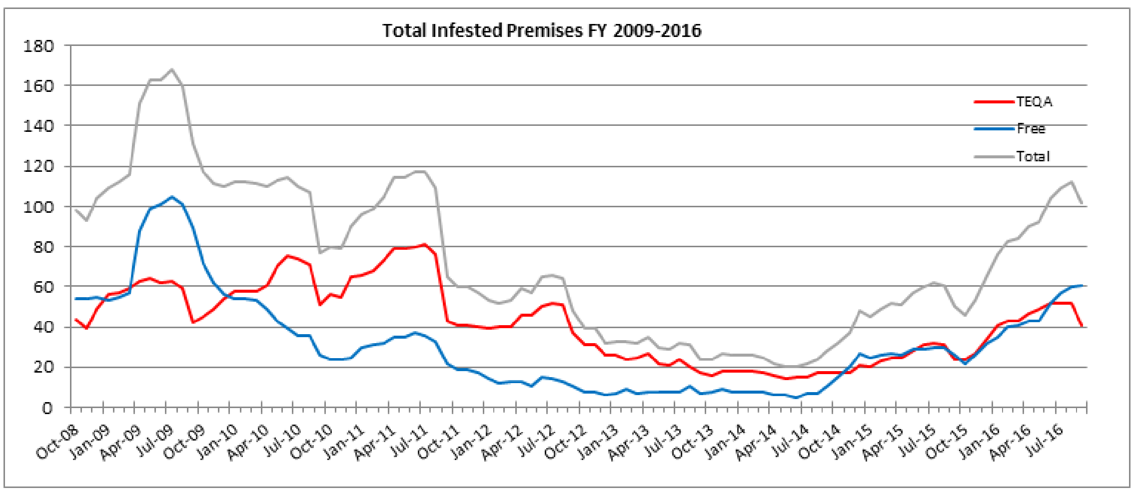

Figure 2. Infested premises in the Tick Eradication Quarantine Area (TEQA; permanent quarantine zone) and outside of the permanent tick quarantine zone (tick free area) from FY 2009-2016.

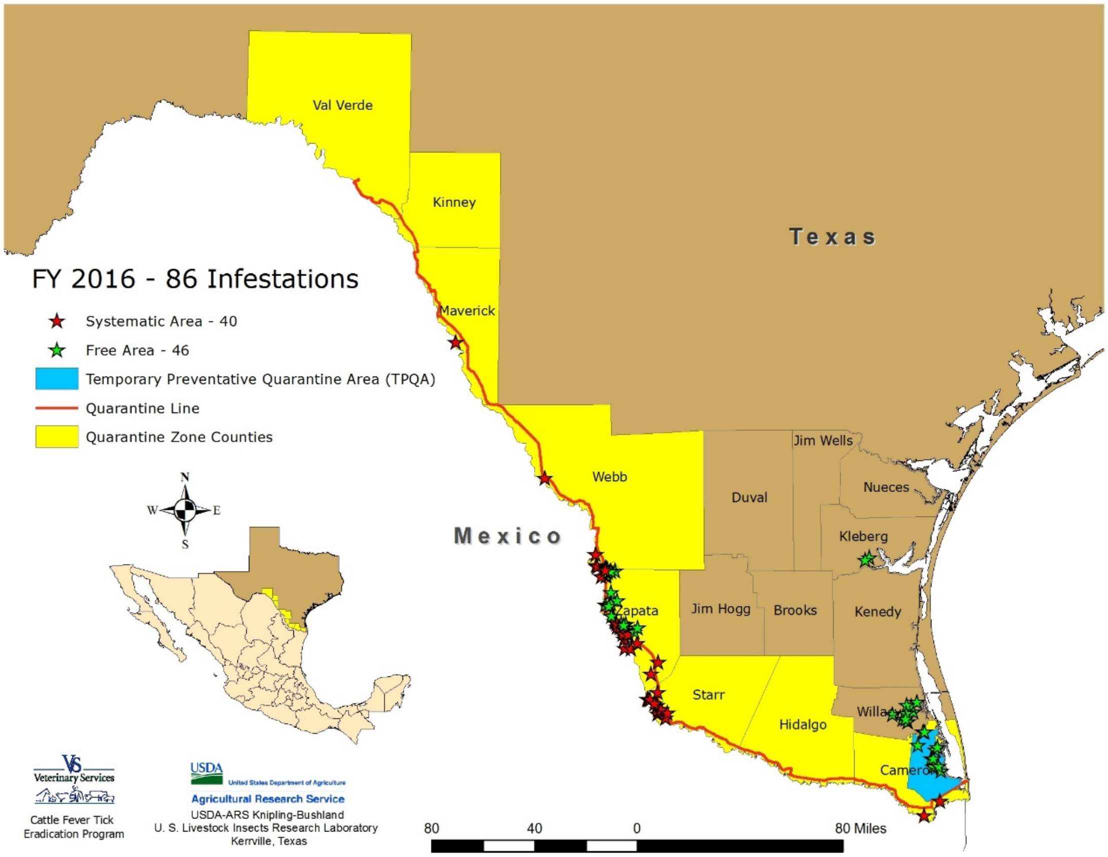

Figure 3. Map of Infestations in Fiscal Year (FY) 2016 highlighting the Quarantine Zone Counties and Temporary Preventative Quarantine Area.

In this environmental assessment (EA), APHIS analyzes the potential impacts on the human environment associated with adding an additional treatment method to the CFTEP. APHIS is proposing to treat white-tailed deer with ivermectin to control tick vectors of cattle fever in Cameron, Hidalgo, Jim Wells, Kinney, Maverick, Starr, Val Verde, Webb, Willacy, and Zapata counties in South Texas (figure 4). White-tailed deer would be fed ivermectin-treated corn from a closed gravity feeder placed in areas where cattle fever is a concern. The information presented in this EA is consistent with requirements in the National Environmental Policy Act of 1969 as amended (42 U.S.C. §§ 4321 et seq.), NEPA regulations promulgated by the Council on Environmental Quality (40 C.F.R. §§ 1500-1508), and APHIS implementing procedures (7 C.F.R. pt. 372).

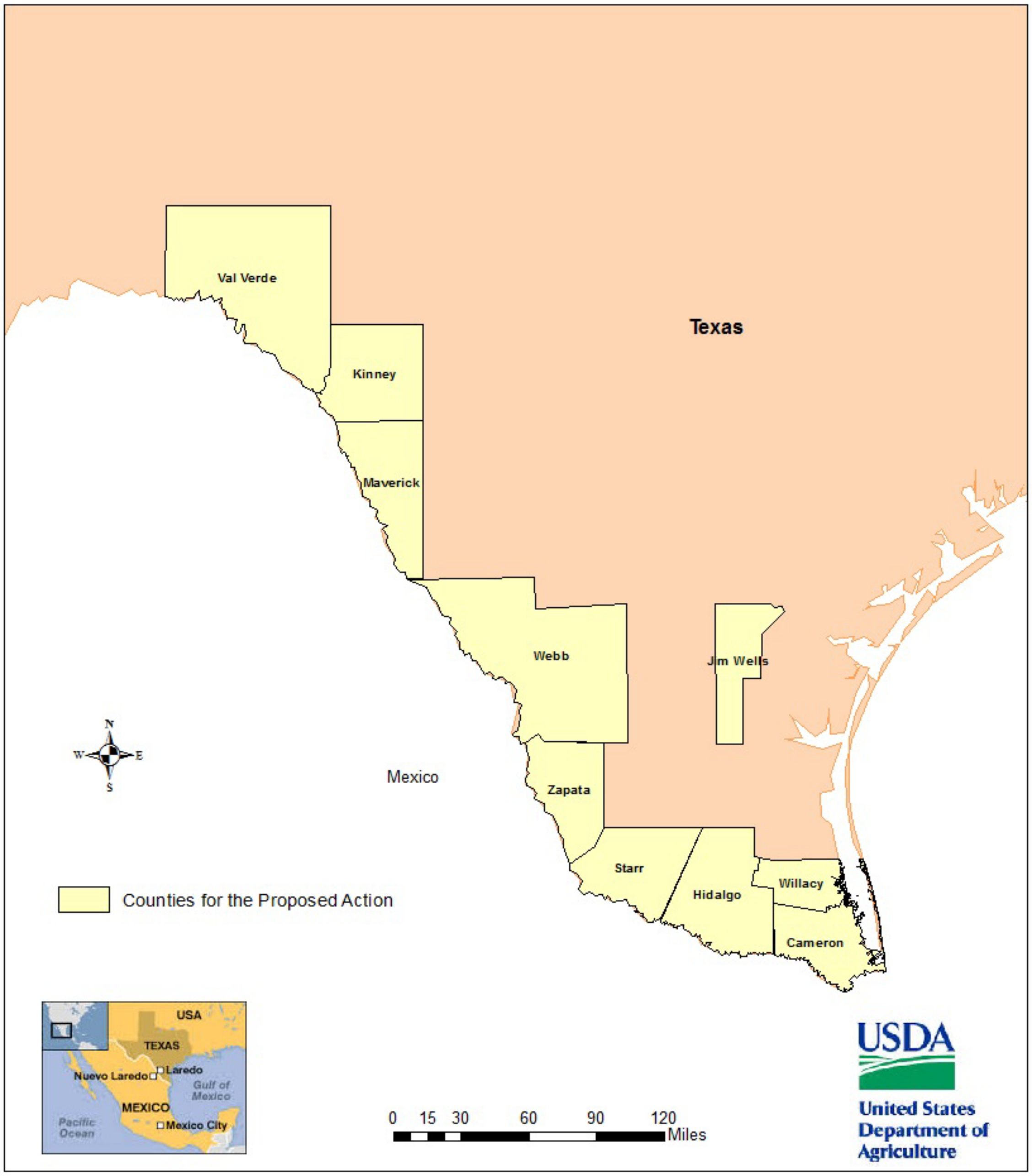

Figure 4. The 10 South Texas counties included in the proposed action.

APHIS uses Ivomec® or Ivomax® pour-on for cattle formulation mixed with whole kernel corn. Ivomec® pour-on for cattle is sold by Merial, Inc., and Ivomax® pour-on for cattle is a generic product (FDA ANADA 200-272). The treated corn is placed in gravity flow feeding stations from February through July to control cattle fever ticks in deer populations (nilgai do not eat corn and thus, are not treated). The gravity flow feeder is a commercially made plastic bin device with four feed tubes below the bin, and a lid (figure 5). Each feeder has a holding capacity of approximately 300-350 pounds of corn. Each feed site will include one gravity flow feeder. In areas with non-target animals (such as hogs, javelina, or livestock) in the vicinity, feeders will be enclosed with welded wire panels to exclude non-target animals. The feeders will be serviced and filled weekly. The program office will maintain records including wildlife treatment feeding/bait station data sheets, service record sheets, and a map showing the number and location of each feeding station (USDA APHIS, 2016a).

Figure 5. Closed gravity feeder system used to dispense ivermectin-treated corn to white-tailed deer.

For dosing, 200 milliliters (ml) of the formulation containing 5 milligrams (mg) ivermectin/ml will be pumped into 100 pounds of clean corn to produce 10 mg of ivermectin active ingredient per pound of corn. The daily intake dose of the deer is approximately 0.22 mg/kilogram (kg) assuming a 100 pound white-tailed deer eats 1 pound of corn per day. A previous study concluded that a feeding rate of 0.22 mg/kg should produce maximum blood serum levels of approximately 30 parts per billion (ppb) (Pound et al., 1996). The target concentration of 30 ppb assures a high degree of efficacy even in those deer that may consume as little as one-third of the targeted dosage. Serum levels of just 10 ppb (one-third of the dosage) should produce 100 percent efficacy against ticks attempting to feed on treated animals (Pound et al., 1996; Nolan et al., 1985; Miller et al., 1989).

The number of feed sites will be determined based on number and density of deer (1 feeder per 20–30 deer to minimize excessive competition and social dominance), and density of feeders per area (deer do not have to travel more than ¼- to ½-mile to access feed = 1 per 125 acres to 1 per 500 acres). In general, ivermectin-treated corn stations are placed in areas of high deer use. Remote sensing data is used to identify areas on the property that are likely to be used by deer. This data is combined with local observation identifying areas with obvious evidence of deer use. More specifically, these areas should show evidence of significant deer utilization such as those areas with high density of deer tracks, high volume of excrement, and heavy browse-line on vegetation. A site for the feeder is selected that is relatively flat and level. There is a minimum 30-foot diameter perimeter barrier around feeders in areas where other large animals could potentially access them.

B. Purpose and Need

In 1968, cattle fever ticks were discovered on white-tailed deer in ranches in Dimmit County, and additional cattle fever ticks were discovered on deer in other areas in later years, raising concern about the role of white-tailed deer in cattle fever tick outbreaks in the tick-free area. Since then, more evidence has been gathered on the role of white-tailed deer as suitable cattle fever tick hosts and their importance in tick eradication efforts.

Numerous studies have shown that white-tailed deer are suitable hosts and reservoirs for cattle fever ticks (Graham et al., 1972, *in* Pound et al., 2010; George, 1990). In the 1970s, chronic cattle fever tick infestations on ranch properties in Webb County north of Laredo, Texas, were not resolved by pasture vacation (Pound et al., 2010). In 1979, after sampling white-tailed deer in an area of Webb County, a study demonstrated that white-tailed deer sustained the existence of and spread cattle fever ticks within pastures vacated of cattle (Gray et al., 1979, *in* Pound et al., 2010). This study reinforced the conclusion from an earlier study (Graham et al., 1972) that white-tailed deer can support cattle fever ticks within vacated pastures and from another study that white-tailed deer distribute the ticks from infested to non-infested pastures.

Failure to control ticks on wildlife hosts greatly compromises efforts to eradicate ticks on livestock and poses a substantial threat of infestation and disease establishment throughout South Texas. In the 1930s, white-tailed deer infestation with cattle fever ticks presented a significant obstacle to cattle fever eradication in Florida (Pound et al., 2010). Dense populations of deer and other wildlife species in South Texas threaten the effort to keep Boophilus spp. ticks from becoming reestablished in the southern United States (George, 1990). Current efforts to control cattle fever ticks on wildlife include a partial tick control barrier fence and population control of certain hosts such as nilgai. Studies show that feeding corn treated with ivermectin to white-tailed deer could also be an effective tool in minimizing the movement and maintenance of cattle fever ticks (Pound et al., 1996; Miller et al., 1989).

To control ticks on deer, APHIS proposes the use of ivermectin-treated whole kernel corn bait in feeding stations to deliver a systemically active acaricide. The U.S. Food and Drug Administration (FDA) does not object to an extra-label drug use as long as all applicable provisions of 21 CFR 530 are met, which includes establishing a withdrawal period that ensures no illegal drug residues occur in treated deer (email from Vitolis E. Vengris, Deputy Director, Division of Surveillance, Center for Veterinary Medicine, U.S. Food and Drug Administration, to Thomas R Kasari, Cattle Health Staff Veterinarian, USDA-APHIS-VS (March 14, 2016 1:00PM DST) on file with APHIS). The CFTEP has a 2015 agreement with the Texas Animal Health Commission (TAHC) and the Texas Parks and Wildlife Department (TPWD) for treating wildlife hosts for cattle fever ticks by feeding them with an ivermectin-treated corn product (Memorandum of Understanding between TAHC and TPWD and USDA APHIS VS (Dec. 2, 2015) on file with APHIS).

II. Alternatives

A. No Action

Under the no action alternative, APHIS would not place ivermectin corn in feeders in Cameron, Hidalgo, Jim Wells, Kinney, Maverick, Starr, Val Verde, Webb, Willacy, and Zapata counties in South Texas to minimize the spread of cattle fever ticks by white-tailed deer. APHIS would continue to carry out current activities that help prevent the spread of ticks and potential exposure of cattle to babesiosis. These activities include inspection of livestock at selected South Texas markets handling livestock originating from the Permanent Tick Quarantine Zone, patrols for stray or smuggled livestock in the Permanent Tick Quarantine Zone along the Rio Grande, inspection and pesticide treatment of tick-host livestock (mostly cattle and horses) on quarantined premises, and nilgai removal.

B. Ivermectin-treated Corn (Preferred Alternative)

Under the preferred alternative, APHIS would strategically place ivermectin-treated corn in feeders on private and public lands in Cameron, Hidalgo, Jim Wells, Kinney, Maverick, Starr, Val Verde, Webb, Willacy, and Zapata counties. Ivermectin-treated corn would most likely be used in locations where cattle fever ticks have been detected along the permanent quarantine line, or in adjacent areas of those counties that are determined to be at risk of incurring an infestation due to movements of tick-infested deer. Jim Wells and Willacy counties are included as part of the potential action area to prepare in advance that ivermectin corn can be used in these counties in the event that cattle fever ticks are detected there. The use of ivermectin corn will serve as an additional tool in needed areas to help CFTEP personnel prevent cattle fever tick infestations beyond the Permanent Tick Quarantine Zone. The CFTEP surveillance, population reduction, and eradication activities described under the no action alternative would continue.

III. Potential Environmental Impacts

In this chapter, APHIS summarizes the potential impacts to the physical, biological, and human environment of Cameron, Hidalgo, Jim Wells, Kinney, Maverick, Starr, Val Verde, Webb, Willacy, and Zapata counties in South Texas. The affected environment as described in the CFTEP DEIS (USDA APHIS, 2013) for Maverick, Starr, Webb, and Zapata counties is incorporated by reference.

A. No Action

1. Physical Environment

According to the Texas State Historical Association, Jim Wells, Kinney, Maverick, Webb, and Zapata county lies within an area designated as the Rio Grande Plain. The Rio Grande Valley includes Cameron, Hidalgo, Starr, and Willacy Counties, while Val Verde is part of the Edwards Plateau (figure 6; TSHA, 2015). As part of the Coastal Plain Physiographic Province in Texas, this region's mean annual soil temperature regime is hyperthermic, and the soil moisture regime is aridic. Entisol, Inceptisol, Mollisol, and Vertisol soil orders dominate (TAMU, 2014). Soils are fine- to coarse-textured, well drained, with limited soil moisture available for use by vegetation during the growing season (McNab and Avers, 1994). Soils range from alkaline to slightly acidic clays and clay loams. Table 1 summarizes characteristics of each county (TSHA, 2015) not already described in the CFTEP DEIS (USDA APHIS, 2013).

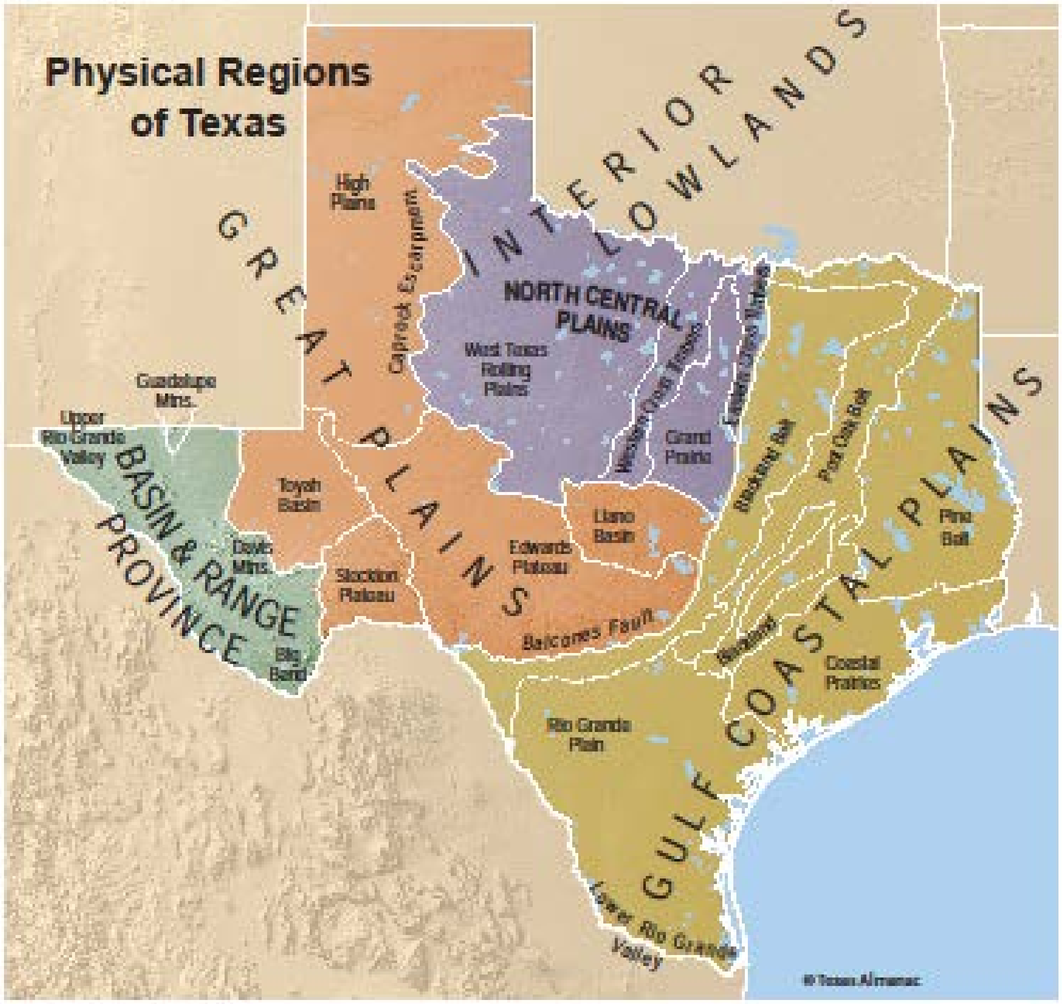

Figure 6. Physical regions of Texas (http://texasalmanac.com/sites/default/files/images/maps/PhysicalReg.pdf) (TSHA, 2015)

Table 1. Summary of County Characteristics (TSHA, 2015)

County	**Area (square miles)**	**Elevation above sea level (feet)**	**Soil types in most of the county**	**Vegetation**
Cameron	905	0-60	Brownish to reddish soils, with loamy to clayey surface layers, and clayey subsoils	Gulf Prairie and Marsh
Hidalgo	1,596	40-200	Sandy and light loamy soils over deep reddish or mottled clayey subsoils; or moderately deep to deep loamy surfaces over clayey subsoils, or brown to red clays	South Texas Plains

County	Area (square miles)	Elevation above sea level (feet)	Soil types in most of the county	Vegetation
Jim Wells	845	200-400	Light to dark, with loamy surfaces over reddish, clayey subsoils over limestone; or gray to black, cracking, clayey soils	South Texas Plains
Kinney	1,359	1,000-2,000	Rocky and hilly with some loamy soils; or gray to black, cracking, clayey soils over limestone with light-colored loamy soils	Edwards Plateau or South Texas Plains
Maverick	1,287	540-960	Gray to black, cracking, clayey soils with high shrink-swell potential; or light-colored loamy soils with limestone bedrock	Mesquite, live oak, cat's claw, huajilla, cenizo, and prickly pear
Starr	1,226	200-400	Sandy or light-colored loamy soils over very deep, reddish, or mottled clayey subsoils; or light-colored, deep to moderately deep, well-drained soils; or gray to black cracking clay	South Texas Plains
Val Verde	3,150	2,248-2,925	Dark, calcareous stony clays and clay loams	Desert shrub; or juniper, oak, and mesquite savanna
Webb	3,363	400-700	Clayey and loamy	Mesquite, grasses, thorny shrubs, and cacti
Willacy	589	0-50	Dark brown to red loam over deep clayey subsoils; or sandy and saline (cracking) along the Gulf Coast	Mesquite, grasses, thorny shrubs, and cacti
Zapata	999	200-700	Light-colored, loamy soils over reddish or mottled clayey subsoils	Mesquite, grasses, thorny shrubs, and cacti

Throughout the proposed action area, the vegetation is relatively consistent except near the coast. The majority of the vegetation in the South Texas Plains area includes live oaks, mesquite, brush, weeds, cacti, and grasses. The Edwards Plateau is predominantly short grasses, mesquite, and cacti. Val Verde County has desert shrub or juniper, oak, and mesquite savanna. Along the Gulf Coast in Willacy County, the vegetation shifts to cordgrasses, seashore saltgrass, and marsh millet. In Cameron County, Gulf Prairie and Marsh vegetation is predominantly marsh grasses, bluestems, and grama grasses (TSHA, 2015).

The climate in South Texas is considered subtropical. Temperatures in the summer are hot, with average high temperatures near 100 degrees Fahrenheit. Winter weather is mild, with average minimum temperatures near 45 degrees Fahrenheit. Precipitation averages approximately 20 inches annually, with more precipitation in the summer than in the winter (table 2). A southerly wind is the predominant wind condition in South Texas. In most areas of the State, the average wind speeds are between 7 and 15 miles per hour (Bomar, 2008).

Table 2. Summary of climatic information (TSHA, 2015)

County	**Temperature (average winter low to average summer high in ^{o}F)**	**Average annual rainfall (in inches)**	**Average growing season (length in days)**
Cameron	50 to 94	26	320
Hidalgo	47 to 96	23	320
Jim Wells	44 to 96	28	304
Kinney	36 to 96	22	272
Val Verde	35 to 97	17	300
Willacy	48 to 95	27	318

Drought has historically been a disturbance in the Rio Grande Plain, and 90 percent of the area has been converted from natural vegetation to dry-land pasture for cattle grazing (McNab and Avers, 1994). According to the U.S. Global Climate Change Research Program (Karl et al., 2009), average temperatures in the Southern Great Plains (Texas) increased across the region, and are projected to continue this increase. Cold days are becoming less frequent and hot days are more frequent. Precipitation is projected to decrease, causing the area to become drier. In 2011, Texas experienced the most intense one-year drought since statewide weather records were initially maintained in 1895 (Nielsen-Gammon, 2011). These climatic trends are expected to shift the ranges of native plants as they become less competitive in areas where they are not well adapted. Weather events affecting soil erosion also are associated with shifts in host plant density, and may alter the ease and frequency of wildlife movements. Therefore, as the area becomes hotter and drier, and water as well as food preferred by wildlife becomes scarcer, wildlife migration has the potential to spread ticks over greater areas. Similarly, drought and higher average temperatures would reduce vegetation available for livestock grazing, which may lead the ranching industry to move northward in search of areas where cattle can thrive with fewer heat impacts. Further climate change in South Texas is likely to create suitable cattle fever tick habitat in northern areas that may not have been suitable for ticks in the past (Perez de Leon et al., 2012). Under the no action alternative, APHIS would not use ivermectin corn to help decrease the potential for ticks to spread into new areas.

Agricultural production in the proposed action area also includes commercial producers of hogs, sheep, and goats located in Cameron, Hidalgo, Kinney, Val Verde, and Willacy Counties. Major crops in Cameron, Hidalgo, and Willacy Counties include sugarcane, grain sorghum, and citrus (Combs, 2008; TSHA, 2015). Onion production in Cameron, Hidalgo, Starr, and Willacy Counties is relatively famous in the United States (Combs, 2008).

All of the counties in the proposed action area are in the Texas Commission on Environmental Quality, Air Quality Control Area Region 14 (Jim Wells), Region 15 (Cameron, Hidalgo, Kinney, Starr, Val Verde, and Willacy), and Region 16 (Maverick, Webb, and Zapata) (https://www.tceq.texas.gov/publications/gi/gi-002.html). South Texas counties tend to have better air quality than many of the other major urban areas around the State (Combs, 2008), although air quality information is not available for Jim Wells, Kinney, Starr, Val Verde, Willacy, and Zapata Counties (U.S. EPA, 2016). From January – September 2016, most of the monitoring in Cameron, Hidalgo, Maverick and Webb Counties found the Air Quality Index (AQI) values were “Good” or “Moderate”. There were 2 days when the AQI values exceeded 100 (rating “Unhealthy for Sensitive Groups”) in Cameron County and 1 in Hidalgo County (U.S. EPA, 2016). Across these four reporting counties, the main pollutants were Particulate Matter 2.5 and Ozone. There was 1 day in Webb County when Particulate Matter 10 was the main pollutant. There were no days that the air quality (in the Texas cities where air quality was measured) in the identified counties exceeded U.S. EPA standards (U.S. EPA, 2016). Additional discussion on air quality is not directly applicable under the circumstances because CFTEP activities are not known to impact air resources.

A watershed is an area of land that contributes water to a river or stream. The overall project area includes reservoirs, streams, rivers, ephemeral (short-lived), intermittent, and perennial drainage features (TCEQ, 2015) that are considered jurisdictional waters of the United States subject to Clean Water Act regulations (40 C.F.R. §§ 136, 230-233). The principal rivers associated with the area of the proposed action include portions of the Rio Grande and Nueces. Minor water bodies include streams and arroyos. The proposed action would be located in or along the (a) Rio Grande watershed, (b) Neuces River Basin watershed, (c) Nueces-Rio Grande Coastal Basin, and (d) the Texas Coastline (the Brownsville Ship Channel and South Bay in Cameron County) (TCEQ, 2015). Major reservoirs in the South Texas Region include the Amistad, Choke Canyon, and Falcon Reservoirs, and the lakes include the Anzalduas Channel Dam, Casa Blanca, Corpus Christi, Delta, Loma Alta, and the Upper Nueces Lake (Combs, 2008). This region relies less on groundwater than surface water supplies, but irrigation accounted for more than 65 percent of the region's groundwater use (Combs, 2008).

Federal activities must seek to avoid or mitigate actions that would adversely affect wild and scenic rivers or areas immediately adjacent to the designated rivers (National Wild and Scenic Rivers Act of 1968, as amended (16 U.S.C. §§ 1271-1287)). There are one hundred ninety-six miles of the Rio Grande extending from Mariscal Canyon to the Terrell/Val Verde County line designated as a wild and scenic river. The habitat associated with this area is not conducive to cattle fever ticks; therefore, APHIS will not be placing ivermectin corn feeders nearby.

There are four major and three minor aquifers in the South Texas region (Combs, 2008). The proposed action will occur several miles away from outcrop parts of the Edwards (in Val Verde and Kinney Counties) and Gulf Coast (in Cameron, Hidalgo, Jim Wells, Starr, Willacy, and Zapata Counties) aquifers, in addition to the southwestern extent of the Carrizo-Wilcox aquifer (in Maverick and Webb Counties) where it lies or dips below other formations (George et al., 2011). Outcrop areas are the part of an aquifer lying at the land surface. Parts of Kinney County are in the Edwards Aquifer, and the remainder is in part of the Edwards-Trinity Plateau aquifer. The only minor aquifer reported within the proposed action area is an outcrop area of the Yegua-Jackson aquifer in Webb, Zapata, and a small portion of Starr County. As of 2010, areas with groundwater conservation districts included Kinney, Jim Wells, and Starr Counties, in addition to small areas in Hidalgo and Willacy Counties. At that time, groundwater management areas placed Val Verde and parts of Kinney in district 7 with the remainder of Kinney in district 10; Maverick, Webb, and Zapata Counties in district 13, with the remainder of Webb County in district 16; and Starr, Hidalgo, Cameron, Willacy, and Jim Wells Counties in district 16 (George et al., 2011). Additional discussion of impairments and sole source aquifers is not directly applicable under the no action alternative because current CFTEP activities are not known to impact water resources.

2. Livestock and Wildlife

The effectiveness of the CFTEP requires an understanding of the roles many organisms play in cattle fever tick infestations and the spread of disease pathogens. All of the tick hosts (primary, alternate, and occasional) may be infected, experience disease, and harbor the protozoan pathogens in addition to suffering blood loss from tick feeding. Tick feeding can transmit a variety of pathogens. Table 3 summarizes the organisms and their roles. To simplify discussion, throughout this EA we refer to cattle fever ticks and diseases to collectively include all the pertinent organisms.

Table 3. Summary of pertinent organisms and their roles in the CFTEP

Common name	**Scientific name**[1]	**Role**
Cattle Fever Ticks	*Rhipicephalus* (*Boophilus*) *annulatus* and *R. microplus*	Pests and vectors of diseases
Protozoan Pathogens	*Babesia bovis* and *B. bigemina*	Causal agents of the disease bovine babesiosis
Rickettsia Pathogen	*Anaplasma marginale* Theiler, 1910	Causal agent of the disease bovine anaplasmosis
Spirochaete Pathogen	*Borrelia theileri* Laveran 1903, Bergey et al., 1925	Causal agent of the disease relapsing fever (borreliosis)
Cattle	*Bos taurus taurus* L., 1758 [Mammalia: Bovidae], *B. taurus indicus* L., 1758	Livestock -- Primary Host
Horse	*Equus caballus* L., 1758 [Mammalia: Equidae]	Used by inspectors, ranch hands, and landowners Livestock -- Primary Host
Axis deer	*Axis axis* Erxleben, 1777 (*Cervus axis*) [Mammalia: Cervidae]	Wildlife or Livestock -- Alternate Hosts
Fallow deer	*Dama dama* L., 1758 [Mammalia: Cervidae]	
Red deer, American elk (or wapiti)	*Cervus elaphus* L., 1758 [Mammalia: Cervidae], *Cervus elaphus canadensis* Erxleben, 1777	
American Bison	*Bison bison* L., 1758 [Mammalia: Bovidae]	
Aoudad sheep	*Ammotragus lervia* Pallas, 1777 [Mammalia: Bovidae]	
White-tailed deer	*Odocoileus virginianus* Zimmerman, 1780 [Mammalia: Cervidae]	Wildlife -- Alternate Hosts
Nilgai antelope	*Boselaphus tragocamelus* Pallas, 1766 [Mammalia: Bovidae]	
Pigs	*Sus scrofa* L., 1758 [Mammalia: Suidae]	Occasional Hosts[2]

Common name	Scientific name[1]	Role
Dogs	*Canis lupes familiaris* L., 1758 [Mammalia: Canidae]	Occasional Hosts
[1]Taxonomic information from ITIS online database, last accessed Oct. 13, 2015 http://www.itis.gov. [2] Wild pigs and dogs exhibit limited potential to spread ticks (Barros and Fighera, 2008).		

One of the greatest concentrations of exotic animals in Texas occurs within the South Texas Plains ecoregion. Free-ranging exotic species in Texas include blackbuck and nilgai antelope; axis, fallow, and sika deer; aoudad and mouflon sheep; feral swine (Sheffield, 2013), and red deer or wapiti (Pound et al., 2010) (see table 3). The identification of exotic species as tick hosts presents a threat to the CFTEP by compromising the success of ongoing eradication efforts. Reducing population levels of potential hosts limits the likelihood that cattle fever tick host populations will move northward and spread cattle fever ticks into new regions.

TPWD controls “Wildlife Management Areas” (WMA) in portions of Cameron, Hidalgo, Starr, and Willacy Counties as part of the Las Palomas WMA, Lower Rio Grande Valley Units. The 3,311 acres of land in the Las Palomas WMA preserves native brush nesting habitat, some farmland, and wetlands for white-winged doves. There are 18 units with tracts ranging from two to 604 acres in size. Las Palomas WMA features hiking, hunting, and wildlife viewing (TDPW, 2016). There are no WMA in Jim Wells, Kinney, Maverick, Val Verde, Webb, and Zapata counties (TDPW, 2016).

Impacts from a spreading cattle fever tick infestation could occur beyond Cameron, Hidalgo, Jim Wells, Kinney, Maverick, Starr, Val Verde, Webb, Willacy, and Zapata Counties. States, counties, and areas without an active tick or disease eradication program may find herds and breeding stock become infested by ticks or infected with diseases during trade. Consequently, indirect impacts associated with the No Action alternative include the likelihood that, without the use of ivermectin corn, States other than Texas may need to create their own tick eradication programs, alter conditions of sale for herds and breeding stock, reactivate regulations previously used to deal with cattle fever ticks and diseases, or create precautionary measures restricting trade.

3. Human Environment

Human populations in the identified counties include residents, hunters, ranchers, and CFTEP employees. Residents include but are not limited to adults and children living in Colonias. Exposure to various ticks is unlikely for most residents during the course of their normal activities. There is an increased risk of exposure to ticks when children and adults participate in outdoor activities, and the overall risk of exposure to ticks may increase under the no action alternative as a result of untreated deer that could maintain many varieties of ticks. However, the risk of exposure to cattle fever ticks, specifically, is minimal because humans are not a host for these ticks.

Hunters experience increased risk of tick exposure during their hunting seasons. In general, tick exposure by ranchers is highly unlikely during the course of their normal activities on uninfested lands. Ranchers and those working with livestock are at increased risk of tick exposure when they travel across tick-infested areas or encounter infested stray livestock or wildlife. If tick populations establish in their pastures, then exposure of people working with livestock in those areas is likely. Exposure to ticks occurs for CFTEP and TAHC employees during the course of their work duties; however, risk of exposure to cattle fever ticks is minimal because they do not infest humans.

The demographics for this area of South Texas indicate the overall population has a large proportion of Hispanics who are likely to have graduated high school, but are not likely to speak English at home (table 4). In general, county-level poverty estimates are not comparable to other geographic levels (state or national) because the poverty estimates may come from sample data with associated sampling errors (e.g. see table 4 footnote 2). Nevertheless, roughly 20 to 40 percent of the population in each county in the proposed program area appears to be below the poverty level.

Table 4. Select Demographics in the Program Area.

Location	**Total population**[1]	**Percent white**	**Percent Hispanic (all races)**	**Percent language other than English at home**	**Percent high school graduate or higher**	**Percent below poverty level**[2]
State of Texas	26,956,958	80.0	38.6	34.7	81.2	17.6
Counties within Texas						
Cameron	420,392	97.2	88.7	73.1	63.7	32.4
Hidalgo	831,073	97.0	91.2	84.9	61.8	34.0
Jim Hogg	5,255	97.2	91.6	81.9	66.1	24.0
Kinney	3,526	94.4	56.5	58.1	68.9	19.3

Location	Total population[1]	Percent white	Percent Hispanic (all races)	Percent language other than English at home	Percent high school graduate or higher	Percent below poverty level[2]
Maverick	57,023	96.9	95.1	94.2	56.6	24.4
Starr	62,955	98.8	95.8	95.6	45.0	36.3
Val Verde	48,974	95.2	80.4	72.2	67.0	23.9
Webb	266,673	97.6	95.2	91.3	64.2	30.6
Willacy	21,903	95.3	87.7	45.4	62.2	43.1
Zapata	14,319	98.7	93.9	87.2	54.8	29.5
[1]Based on U.S. Census Bureau data from 2014 estimates (Total Population) or 2009-2013 (other categories), last accessed Nov. 6, 2015 http://quickfacts.census.gov/qfd/states/48000.html. [2]Based on the official poverty definition that uses monetary income before taxes and does not include capital gains or noncash benefits (such as public housing, Medicaid, and food stamps). If the total income for a family is less than the threshold, then that family (and every individual in it) is considered in poverty.						

An increase in the number of cattle fever tick infestations over an increasingly large area could result in adverse economic and health impacts on affected producers and consumers, such as higher consumer prices, loss of local employment, reduced nutritional options, loss of market share, compromised mental and physical health, loss of property, and so on. These indirect impacts are likely to occur to a lesser extent under the preferred alternative.

B. Preferred Alternative

1. Physical Environment

Short-term disturbances to soil, water, vegetation, or air resources could occur, but are unlikely, as a result of the use of ivermectin-treated corn. Theoretically, greenhouse gas release occurs during the routine use of vehicles and the production of ivermectin used for the program. Ivermectin has low volatility and is unlikely to partition into the atmosphere.

Ivermectin binds strongly to soil particles making it unlikely to leach into groundwater or runoff to surface water in a dissolved state (USDA APHIS, 2016b). Ivermectin breaks down to less bioactive compounds via photo and aerobic degradation; degradation in soil varies with the soil type and properties, sorption capacity, and temperature (USDA APHIS, 2016b). Ivermectin half-lives in soil are 7 to 14 days at high temperatures in summer, but can be much longer (91 to 217 days) at low temperatures in the winter. Photolysis in water is less than 0.5 day in summer, and 39 hours in winter. When directly exposed to sunlight, its photolytic half-life was approximately 3 hours on a thin, dry film (USDA APHIS, 2016b). In addition, studies in cotton and food crops (sorghum, lettuce, carrots, and turnips) show that plants uptake little ivermectin from direct applications to plants or from soil (USDA APHIS, 2016b).

2. Livestock and Wildlife

Ivermectin is absorbed into blood, distributed throughout the mammal's body, and deposited in the body fat and liver (USDA APHIS, 2016b). The absorption rate varies with the route of administration, formulation, and animal species. Ruminant species appear to have a slower absorption process than monogastric animals. The safety data sheet for formulated ivermectin reports oral LD_{50} values for ivermectin component B1a and component B1b are ~80 mg/kg (dog), 25 mg/kg (mouse), 50 mg/kg (rat), and higher than 24 mg/kg (rhesus monkey) (USDA APHIS, 2016b).

Ivermectin blocks the transmission of neural signals of the parasites by binding selectively and with high affinity to the glutamate-gated chloride channels in nerve and muscle cells of invertebrates, and acting as an agonist of the gamma-aminobutyric acid (GABA) neurotransmitter in the peripheral nervous system of invertebrates. However, ivermectin has low toxicity in mammals because GABA is found only in the central nervous system of mammals and is protected by the blood-brain barrier. There are greater toxic effects from ivermectin reported in some dog breeds such as collies and sheepdogs, because these breeds carry a mutation of the multiple drug resistance gene (MDR1) causing an abnormality in the blood-brain barrier that allows increased ivermectin into the central nervous system (USDA APHIS, 2016b).

Ivermectin is considered highly toxic to most aquatic invertebrates; however, the proposed method of application, program controls, and environmental fate of ivermectin suggest there will not be significant exposure in aquatic habitats. Ivermectin is used as a therapeutic treatment for fish and amphibians with 96-hour LC_{50} values ranging from 3.3 to 5.3 µg/L for the rainbow trout, *Onchorynchus mykiss*, and bluegill sunfish, (*Lepomis microchirus*) respectively (USDA APHIS, 2016b).

APHIS expects ivermectin risks to most fish and wildlife species to be very low. There is the possibility of exposure to some non-target terrestrial wildlife who may consume corn spilled onto the ground during feeding by white-tailed deer. The use of exclusion barriers (welded wire panels precluding swine, javelin, and livestock) combined with weekly monitoring of the feeders reduces this potential exposure. The low probability of exposure and administration of therapeutic doses of ivermectin suggest that risk to non-target terrestrial vertebrates who may consume some spilled treated corn will be low.

There is some risk to terrestrial invertebrates, such as beetles and flies, if they solely depend on droppings from white-tailed deer for development. Studies show that approximately 90 percent of the ivermectin dose administered parenterally or orally is excreted in the feces (USDA APHIS, 2016b). Localized impacts to this group of invertebrates depend on site-specific conditions influencing ivermectin degradation and availability (USDA APHIS, 2016b).

3. Human Health and Safety

Human health risks associated with the use of ivermectin-treated corn in feeding stations to control cattle fever ticks in deer populations are determined based on the toxicity of ivermectin, and the potential for exposure. The potential for exposure depends on APHIS' proposed application method and the environmental fate profile for ivermectin.

As previously noted in the Livestock and Wildlife section, ivermectin has low toxicity in mammals because GABA is found only in the central nervous system of mammals and is protected by the blood-brain barrier. Therefore, ivermectin is sometimes used as a human drug for the treatment of strongyloidiasis and onchocerciasis in the United States (FDA, 2016), and the treatment of scabies, lice, and ascariasis in other countries (NIDDK, 2016). The FDA-approved ivermectin human drugs currently include Stromectol® (3 milligram (mg) oral tablet), Sklice® (0.5% topical lotion), and Soolantra® (1% topical cream) (FDA, 2016).

Ivermectin can be toxic to humans if accidental overdose or significant exposure to veterinary formulations occurs. The reported adverse human health effects include rash, edema, headache, dizziness, asthenia, nausea, vomiting, and diarrhea (USDA APHIS, 2016b). Exposure to the Ivomax® pour-on formulation may cause the following adverse effects: 1) eye irritation (direct eye contact); 2) irritation and/or drying and cracking of the skin (prolonged or repeated contact); 3) mild irritation of the nose and throat (vapor exposure of isopropyl alcohol in the formulation) and nausea, headache and mild narcosis (prolonged exposures to isopropyl alcohol vapor above the occupational exposure standard); 4) decreased activity, slow rate of breathing, dilation of the pupils, muscle tremors, and in-coordination (overexposure to ivermectin); and 5) burning of the gastrointestinal tract, nausea, vomiting and central nervous system depression (ingesting a large amount of isopropyl alcohol) (Aspen, 2013). The safety data sheet for the Ivomec pour-on for cattle formulation reports oral LD_{50} for ivermectin comp. B1a and comp. B1b is greater than 15 mg/kg (adult human) (Merial, 2010). In humans, ivermectin metabolism occurs in the liver by cytochrome P450 enzymes. Deposition tends to occur in body fat and the liver, where it is progressively metabolized until excreted. Approximately 90 percent of excretion occurs in feces, less than 2 percent in urine, and less than 2 percent in breast milk (USDA APHIS, 2016b).

Humans with potential exposure to ivermectin-treated corn include livestock feed mill employees formulating the medicated corn, program workers filling feeders, and the general public living in the vicinity of feeding stations. Occupational exposure to ivermectin may occur through oral, inhalation, and dermal contact. However, direct contact to ivermectin during outdoor application in well ventilated areas is not expected to occur under normal conditions with proper worker hygiene and properly functioning personal protective equipment (PPE). Drift from the application of ivermectin will not occur because ivermectin has low volatility and corn is loaded directly into the gravity flow feeders. In addition, APHIS program workers are licensed pesticide applicators who understand the risks associated with pesticide use and disposal.

For the general public, potential direct exposure to ivermectin-treated corn is unlikely based on the method of application and program requirements that restrict access to feeders (USDA APHIS, 2016b). Feeders are strategically placed on private properties that will have a restricted access point. Comparable security will be provided at refuges and other public sites. A sign in both English and Spanish will be posted if feeders are placed on public lands. Feeders are checked weekly so that damaged feeders can be repaired or removed, reducing the potential for exposure to the public from corn that may spill onto the ground if the feeder is damaged. Therefore, the potential exposure for the general public to ivermectin via inhalation, dermal exposure, or through ingestion of treated corn is not expected. There is potential for a person to ignore the signage and breach the exclusion fencing to access treated corn due to the fence's height of 34 inches, however, in general, risk to the general public from direct contact exposure to ivermectin-treated corn in feeders in restricted access feeding stations is expected to be low.

Potential exposure of the general public from dietary consumption of meat from ivermectin-treated deer is unlikely because APHIS will discontinue feeding deer with ivermectin-treated corn 60 days prior to the deer-hunting season. The proposed treatment period is annually from February through July. The withdrawal time of 60 days allows ivermectin residues to decrease to below the tolerance levels in white-tailed deer (USDA APHIS, 2016b). Consequently, risks to the general public from dietary consumption of ivermectin in harvested deer meat is expected to be negligible.

Potential exposure of the general public from dietary consumption of meat from feral swine that have ingested ivermectin-treated corn is unlikely because of the installation of exclusion fencing, the design of feed ports, and the time of year associated with hunting swine for food. Feeders will be enclosed with welded wire panels to exclude non-target animals, such as hogs, and serviced weekly. The exclusion fencing surrounding each deer feeder has a height of 34 inches, which is optimum to prevent feral swine from accessing the corn feeders (Rattan et al., 2010). However, while uncommon, breach of fencing by feral swine could occur (Cooper and Ginnett, 2000). When a breach occurs, the program will repair the fencing and report the finding to landowners for them to implement lethal feral swine population control measures (D. Baca, pers. comm., email dated Oct. 19, 2016). The feed ports on the feeders are not easily accessible to feral swine because they are above ground level with a small opening and ventral lip to minimize spillage. The available corn to feral swine if they breach the fencing is minimal—it is estimated that there is less than 5% of the total treated corn in the feeder that ends up on the ground (D. Baca, pers. comm., email dated Oct. 19, 2016). Although hunting for feral swine is allowed year round, APHIS has observed most of the hunting for human consumption occurring during the colder months of the year, generally from November through February. Hunting does occur during the warm to hot months of the year, but this is mostly for population control and trophy hunts for mature boars; meat is not usually salvaged.

There are no anticipated threats to ground and surface water that may be used as drinking water because of the proposed treatment method and environmental fate of ivermectin. Feeding stations are placed a minimum of 50 feet from any aquatic areas and it is unlikely that any treated corn would be transported during a rain event to any surface water source used for drinking water. Small amounts of ivermectin may be released to the soil in deer droppings; however, ivermectin concentrations in soil would be extremely low due to the small amounts of droppings in a given area. In addition, ivermectin is unlikely to leach into groundwater or runoff to surface water because it binds to soil and has low solubility, and will further degrade in environment.

Overall, the use of ivermectin-treated corn in feeding stations to control cattle fever ticks is expected to pose minimal risks to human health under the APHIS proposed applications in the preferred alternative.

4. Wildlife Protections

a. Endangered Species Act

Section 7 of the Endangered Species Act (ESA) and its implementing regulations require Federal agencies to ensure that their actions are not likely to jeopardize the continued existence of endangered or threatened species or result in the destruction or adverse modification of critical habitat. There are 26 federally listed species and species proposed for listing in the program area (Cameron, Hidalgo, Jim Wells, Kinney, Maverick, Starr, Val Verde, Webb, Willacy, and Zapata Counties).

Potential effects of the proposed action to listed species and critical habitat include toxicity of ivermectin to non-target species, removal of brush that serves as species habitat from areas where feeders are placed, runoff of ivermectin into aquatic areas, trampling of listed plants, and species disturbance by feeder set up and weekly servicing.

APHIS has determined that the proposed action may affect, and is likely to adversely affect, the Gulf Coast jaguarondi (*Puma yagouaroundi cacomitli*), ocelot (*Leopardus pardalis*), northern aplomado falcon (*Falco femoralis septentrionalis*), and whooping crane (*Grus americana*). APHIS requested formal consultation with the U.S. Fish and Wildlife Service (FWS) for these species.

APHIS has determined that the proposed action may affect, but is not likely to adversely affect the black-capped vireo (*Vireo atricapilla*), golden-cheeked warbler (*Setophaga chrysoparia*), Devils River minnow (*Dionda diaboli*) and its critical habitat, ashy dogweed (*Thymophylla tephroleuca*), black lace cactus (*Echinocereus rechenbachii var. albertii*), least tern (*Sternula antillarum*), South Texas ambrosia (*Ambrosia cheiranthifolia*), star cactus (*Astrophytum asterias*), Texas ayenia (*Ayenia limitaris*), Texas snowbells (*Styrax platanifolius subsp. texanus*), Tobusch fishhook cactus (*Sclerocactus brevihamatus subsp. tobuschii*), Walker's manioc (*Manihot walkerae*), and Zapata bladderpod (*Lesquerella thamnophila*). FWS concurred with these determinations.

APHIS has determined that the the proposed action will not jeopardize the continued existence of the Texas hornshell (*Popenaias popeii*), a mussel that is proposed for listing as an endangered species.

APHIS has determined that the proposed action will have no effect on the West Indian manatee (*Trichechus manatus*) and its critical habitat, piping plover (*Charadrius melodus*), red knot (*Calidris canutus*), critical habitat of the whooping crane, hawksbill sea turtle (*Eretmochelys imbricata*), Kemp's Ridley sea turtle (*Lepidochelys kempii*), leatherback sea turtle (*Dermochelys coriacea*), loggerhead sea turtle (*Caretta caretta*), and critical habitat of Zapata bladderpod.

APHIS will avoid adverse effects by surveying potential feeder sites for presence of listed plants and nesting birds, placing feeders in areas already dominated by non-native vegetation, avoiding creation or widening of trails to access feeders, implementing buffers for feeder placement from aquatic areas, avoiding removal of native vegetation and brush, avoiding placement of feeders within designated critical habitat, and using feeders that prevent access to treated corn by non-target species. APHIS outlined these mitigations in its biological assessment and submitted it to the FWS, Texas Coastal Ecological Services Field Office.

FWS issued a biological opinion in January 2017 indicating that the proposed use of ivermectin-treated corn in feeding stations will not likely jeopardize the continued existence of the ocelot, Gulf coast jaguarundi, northern aplomodo falcon, or whooping crane. Terms and conditions included in the biological opinion outline reporting and monitoring requirements. Terms and conditions include:

1) information regarding reporting take of an ocelot, jaguarundi, northern aplomado falcon, or whooping crane to FWS;
2) a requirement for APHIS to provide ESA training to all CFTEP personnel;
3) a protocol for use of game cameras to monitor wildlife visiting the ivermectin corn feeders;
4) a requirement for bi-annual ivermectin sensitivity testing of ticks, and;
5) how to submit annual reports to FWS.

The biological assessment (prepared by T. Willard, USDA-APHIS, October 17, 2016) and the biological opinion (including concurrence on "not likely to adversely affect" species) (prepared by E. Reyes, FWS, Ecological Services, January 2017) are included in the administrative record for this EA.

b. Migratory Bird Treaty Act

Federal law prohibits an individual to pursue, hunt, take, capture, kill, attempt to take, capture or kill, possess, offer for sale, sell, offer to purchase, purchase, deliver for shipment, ship, cause to be shipped, deliver for transportation, transport, cause to be transported, carry, or cause to be carried by any means whatever, receive for shipment, transportation or carriage, or export, at any time, or in any manner, any migratory bird or any part, nest, or egg of any such bird (16 U.S.C. §§ 703-712; 50 CFR § 21).

Texas occurs within the Central Flyway, a bird migration route that is composed of the States of Montana, Wyoming, Colorado, New Mexico, Texas, Oklahoma, Kansas, Nebraska, South Dakota, and North Dakota, and the Canadian provinces of Alberta, Saskatchewan, and the Northwest Territories. Many of the migratory bird species of the Central Flyway winter in Central and South America. Some migrate across the Western Hemisphere to the Arctic Circle, and others migrate to South America (NAS, 2016a). Birds in this flyway include the American oystercatcher (*Haematopus palliatus*), black skimmer (*Rynchops niger*), brown pelican (*Pelecanus occidentalis*), greater sage-grouse (*Centrocercus urophasianus*), least tern, lesser prairie chicken (*Tympanuchus pallidicinctus*), piping plover, reddish egret (*Egretta rufescens*), redhead (*Aythya americana*), red knot, ruddy turnstone (*Arenaria interpres*), sanderling (*Calidris alba*), sandhill crane (*Grus canadensis*), whooping crane, and Wilson's plover (*Charadrius wilsonia*) (NAS, 2016a). Birds that migrate along this route depend on stopover habitat, such as native prairie and wetland areas.

Disturbance of nesting migratory birds is not expected because APHIS will not remove brush or native vegetation that migratory birds would use as nesting substrate; as much as possible, feeders will be placed in areas dominated by bare ground, buffelgrass, or other not native vegetation. APHIS will place feeders a minimum of 50 feet from aquatic areas to avoid disturbance of nesting shorebirds from placement and servicing of feeders.

Exposure and toxicity of ivermectin is another potential effect to migratory birds. APHIS prepared an environmental risk assessment for ivermectin-treated corn that is included in Appendix 1 of this document. The risk assessment concluded that direct risk to non-target birds is expected to be low based on the method of application for ivermectin-treated corn and low toxicity of ivermectin to birds. The use of the closed gravity feeder will reduce risk to most terrestrial non-target birds and other animal species. APHIS will place feeders a minimum of 50 feet from aquatic areas to prevent ivermectin runoff that could affect fish and invertebrate prey. Insectivorous birds would not likely ingest ivermectin-treated corn. Small insects that would serve as prey for these birds are also not expected to ingest ivermectin-treated corn. If birds were to ingest the treated corn or prey that has ingested ivermectin-treated corn, acute toxicity of ivermectin to birds is low to moderate depending on the species. The oral median lethal dose (LD_{50}) for ivermectin to bobwhite quail (*Colinus virginianus*) is 2,000 milligrams (mg)/kilogram (kg) and 88 mg/kg for the mallard duck (*Anas platyrhynchos*). Similar sensitivities are seen in dietary studies, with median lethal concentration (LC_{50}) values of 3,102 and 383 mg/kg, for the bobwhite quail and mallard, respectively (Bloom and Matheson, 1993).

c. Bald and Golden Eagle Protection Act

The Bald and Golden Eagle Protection Act (16 U.S.C. 668-668c) prohibits anyone, without a permit issued by the Secretary of the Interior, from "taking" bald eagles (*Haliaeetus leucocephalus*), including their parts, nests, or eggs. The Act provides criminal penalties for persons who "take, possess, sell, purchase, barter, offer to sell, purchase or barter, transport, export or import, at any time or any manner, any bald eagle ... [or any golden eagle], alive or dead, or any part, nest, or egg thereof." The Act defines "take" as "pursue, shoot, shoot at, poison, wound, kill, capture, trap, collect, molest or disturb."

Golden eagles (*Aquila chrysaetos*) are rare to locally uncommon in the Panhandle and western Trans-Pecos area, and very rare to casual throughout the remainder of Texas (Lockwood and Freeman, 2004). For bald eagles, breeding populations occur mainly in the eastern half of the state and along coastal counties from Rockport to Houston (TPWD, undated). Nonbreeding populations of bald eagles are found mainly in the Panhandle, Central, and East Texas, and in other suitable habitat throughout Texas (TPWD, undated). FWS does not indicate that bald eagles occur in any of the 10 program counties (FWS, 2016). Because bald and golden eagles are unlikely to be in the program area, activities associated with ivermectin-treated corn are not expected to cause disturbance to eagles.

Bald eagles in Texas commonly eat coots, catfish, rough fish, and soft-shell turtles (TPWD, undated). Carrion is also common in the diet of bald eagles, especially in younger birds (TPWD, undated). Golden eagles eat a variety of foods, mainly mammals ranging in size from ground squirrels up to prairie-dogs, marmots, and jackrabbits (NAS, 2016b). They may also prey on smaller rodents, birds, snakes, lizards, large insects, and carrion (NAS, 2016b). Should bald or golden eagles occur in an area where ivermectin-treated corn feeders are placed, direct risk to them from feeding on prey that has fed on ivermectin-treated corn is expected to be low because of the method of application for ivermectin-treated corn and low toxicity of ivermectin to birds (see the Migratory Bird Treaty Act section for additional toxicity information). The use of the closed gravity feeder will reduce exposure to most non-target birds and other animal species that could serve as prey to eagles. In addition, eagles would have other food sources that would not contain ivermectin residues, further reducing risk to them. Ivermectin is used therapeutically to treat raptors, including bald and golden eagles, for helminth parasites (parasitic worms, such as tapeworms and roundworms) (Smith, 1993).

5. Environmental Justice

Federal agencies identify and address disproportionately high and adverse human health or environmental effects of its proposed activities as described in Executive Order 12898, “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations,” and Executive Order 13045, “Protection of Children from Environmental Health Risks and Safety Risks.” Adverse direct or indirect effects on vulnerable populations are not likely to occur when there is proper handling of the treated corn combined with an effective communication with program area residents.

Federal agencies must ensure their programs and activities are accessible to persons with limited English proficiency as directed by EO 13166. To meet this need, APHIS conducts outreach to English-speaking and Spanish-speaking communities through a variety of public notices and informational brochures about CFTEP program activities. APHIS will invite all stakeholders, including Colonia ombudspersons and residents of Colonias, to any public meetings. If this EA leads to a finding of no significant impact (FONSI), then APHIS will provide a Spanish translation of the FONSI to program and TAHC representatives for their use when working with the public. In addition, if a FONSI is reached, APHIS will also notify the Director of the Colonia Initiatives Program in South Texas about the new CFTEP activities.

6. Tribal Consultation and Coordination

APHIS met with representatives of the Kickapoo Tribe on February 4, 2013 to review the Tribe’s needs, interests, and concerns (Roberta Duhaime, pers. comm., 30 January, 2014). The Texas Kickapoo Indian Reservation in Maverick County includes 125 acres of trust land along the Rio Grande, an additional 13,000 acres in Maverick County, and has an interest in a 9,000 acre cattle ranch in Spofford, Texas. This is the only federally-recognized tribe reported in the 10 county region, using the Native American Graves Protection and Repatriation Act Online Databases (NPS, 2013; 25 U.S.C. §§ 16 3001 et. seq.). While conducting scoping for the CFTEP DEIS (USDA APHIS, 2013), APHIS contacts with the Tonkawa Tribe of Oklahoma (which once inhabited this area of Texas) indicated their interests extend only to the disposition of artifacts that may be inadvertently uncovered. The proposed action will not disturb the ground, so it is unlikely to affect Native American sites or artifacts. To ensure that tribal communities near the 10 county action area are aware of the proposed action, APHIS mailed the Alabama-Coushatta Tribe of Texas, Ysleta Del Sur Pueblo, and Kickapoo Traditional Tribe of Texas an informational letter inviting further discussions. The letter (prepared by M. Gray, USDA APHIS, November 16, 2016) is included in the administrative record for this EA.

The Archaeological Resources Protection Act of 1979 (16 U.S. Code (U.S.C.) §§ 470aa-mm), secures the protection of archaeological resources and sites on public and tribal lands. If APHIS discovers any archaeological resources, APHIS will notify the appropriate individuals. If the presence of tick-infested animals warrants expansion of the proposed activities onto Tribal lands, program officials will initiate consultation with the governing Tribal authorities and local Tribal Historic Preservation Officers before taking further action.

7. Historic, Cultural, and Visual Resources

The visual resources for the listed counties in Texas are the rangeland and pastures serving as habitat for animals. In general, these counties are of minimal recreational or scenic interest except for areas directly along the Rio Grande River. Hunting occurs in some areas. The visual resources also include any buildings, street patterns and road characteristics, view corridors, and vistas.

The National Historic Preservation Act of 1966, as amended (16 U.S. Code § 470 et seq.), requires Federal agencies to consider the impact on properties included in, or eligible for inclusion in, the National Register of Historic Places (36 Code of Federal Regulations §§ 63 and 800). APHIS identified the listed historic places present in each County (Texas Atlas of Historic Places, https://atlas.thc.state.tx.us/), and summarized the findings in table 5. The museums may be inside historic structures or listed as historic places, or both. A full list of historic places considered during the preparation of this EA is available in the administrative record (prepared by E. Sutker, USDA APHIS, October 25, 2016).

Table 5. Summary of the number of listed historic sites present in the 10 Texas action area counties.

County	Nationally Listed Places	Cemeteries	Museums
Cameron	26 (and 4 battlefields)	19	3
Hidalgo	23 (and 1 battlefield)	13	2
Jim Wells	0	4	1
Kinney	2	1	2
Maverick	2	1	0
Starr	9	2	1
Val Verde	3	2	3
Webb	9	3	1
Willacy	1	1	0
Zapata	6	1	0

APHIS' program activities will not alter, change (restore or rehabilitate), modify, relocate, abandon, or destroy any historic buildings, edifices, or nearby infrastructure. Therefore, APHIS program activities will not directly or indirectly alter characteristics of a historic property that qualifies it for inclusion in the National Register of Historic Properties. The listed historic cemeteries may provide habitat corridors for deer and ticks, nevertheless, treated corn will not be placed on the property of any listed historic property. The proposed action will not disturb the ground for construction. This proposed action does not include mowing, herbicidal treatments, or removal of plant material from any site; private land managers and owners will decide if these activities are to occur on the properties they manage. The proposed activities will not use heavy equipment that creates noise levels requiring auditory protection. Any visual, atmospheric, or auditory effects during delivery and consumption of treated corn will be limited in duration, intensity, and area. APHIS initiated consultation with the State Historic Preservation Office (SHPO) for Texas.

8. Potential Cumulative Impacts

The Council on Environmental Quality defines cumulative impacts as "the impact on the environment which results from the incremental impact of the action when added to other past, present, and reasonably foreseeable future actions regardless of what agency (Federal or non-Federal) or person undertakes such other actions. Cumulative impacts can result from individually minor but collectively significant actions taking place over a period of time."(40 CFR § 1508.7).

The CFTEP program along with trail use by other Federal agencies has been associated with minimal impacts to vegetation and soil compaction. Impacts to vegetation and soil occur to a limited degree as a result of CFTEP trail maintenance to survey for cattle coming from Mexico, U.S. Department of Homeland Security use of sites associated with potential illegal border crossings, and FWS trail use to monitor wildlife. Ivermectin corn feeders would be placed in previously disturbed areas resulting in little to no additional native vegetation or soil compaction.

Ivermectin is a widely used anti-parasitic drug in humans, livestock, and pets (Crump and Omura, 2011). There would be increased environmental loading from the use of ivermectin-treated corn for white-tailed deer where there are also ivermectin uses for cattle and other domestic animals. The impacts to white-tailed deer are expected to be incrementally negligible when put in context with other stressors because the dose of ivermectin is considered therapeutic and not intended to result in adverse effects. Domestic animals that are receiving ivermectin for other purposes are also not expected to have cumulative impacts resulting from the proposed use of ivermectin-treated corn because domestic animals will not be able to access the feeders. Cumulative impacts to aquatic organisms will also be negligible because there is an extremely low probability of exposure to aquatic habitats from the proposed use of ivermectin-treated corn (USDA APHIS, 2016b).

Cumulative impacts to human health from the proposed use of ivermectin-treated corn are not anticipated because of the proposed use pattern. Human exposure and risk is very low for the general public. The probability of exposure is greatest for workers who mix and fill the feeders. However, the risk to this group of the population will be negligible based on the low risk of ivermectin when using the appropriate PPE. There is the potential for worker exposure to other chemicals that may be used in the CFTEP. Coumaphos is an organophosphate insecticide used to treat cattle for ticks that may vector cattle fever. The potential for cumulative impacts related to exposure to both pesticides by workers will be reduced by the use of PPE. Cumulative risk to the public from exposure to mixtures of both chemicals is also not anticipated because of the method of application, program controls, and restriction of public access to treatment areas.

Pesticide use in other Federal programs potentially contributes to cumulative impacts with chemicals used in cattle fever tick management. Ongoing APHIS programs in South Texas using pesticides include the Boll Weevil Cooperative Eradication Program and fruit fly control programs. These programs do not treat livestock. Spinosad is a commonly used agricultural insecticide. It is highly unlikely there would be any pesticide drift of spinosad from fields and orchards or groves into livestock production areas where CFTEP activities occur. Subsequently, the probability of exposure to the public and workers to both spinosad and ivermectin at the same time would be very low because of the use patterns and intended target for each pesticide (USDA APHIS, 2016b).

There has been research to show synergistic effects between ivermectin and antibiotics (doxycycline, erythromycin, rifampicin, and azithromycin) in controlling body lice. These interactions are not expected with the proposed use of ivermectin because treatments will be directed at wildlife that would not be receiving antibiotic treatment. These types of mixture exposures would not be anticipated for humans either because of the method of application and other measures to prevent exposure to the public and workers who mix ivermectin with corn and load the feeders (USDA APHIS, 2016b).

In summary, the cumulative impacts associated with the preferred alternative when assessed in relation to the current baseline and past, present, and future activities constitutes a small incremental change to the human environment. Some of these cumulative changes may be positive such as the reduction in cattle fever ticks and the associated economic benefits from having tick-free cattle. To preserve environmental quality for the human population and ecological resources, the CFTEP would minimize potentially negative cumulative impacts by following best management practices. APHIS does not find that any reasonably foreseeable effects caused by the program activities will occur later in time or be farther removed in time.

IV. Agencies Contacted

U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Environmental and Risk Analysis Services
Policy and Program Development
4700 River Road, Unit 149
Riverdale, MD 20737

U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Cattle Fever Tick Eradication Program
Surveillance, Preparedness, and Response Services
Veterinary Services
2150 Centre Avenue
Fort Collins, CO 80526

Texas Animal Health Commission
2105 Kramer Lane
Austin, TX 78758

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Appendix 1. Ivermectin Risk Assessment

Human Health and Ecological Risk Assessment for the Use of Ivermectin-treated Whole Kernel Corn to Control Cattle Fever Ticks in White-Tailed Deer Populations

EXECUTIVE SUMMARY

United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) Veterinary Services (VS) is proposing the use of ivermectin-treated corn in its cattle fever tick eradication program. Cattle fever is a serious disease that poses a threat to U.S. cattle production, in particular in south Texas. The disease is vectored by the cattle fever tick and southern cattle tick that can parasitize livestock and wildlife. A part of the integrated cattle fever tick eradication program (CFTEP) is the treatment of white-tailed deer using the parasiticide, ivermectin, to control both tick vectors of cattle fever. White-tailed deer are fed ivermectin-treated corn from a closed gravity feeder placed in areas where cattle fever is a concern.

USDA APHIS evaluated the potential human health and ecological risks from the proposed use of ivermectin and determined that the risk to human health and non-target fish and wildlife is low based on the potential for exposure, and the toxicity and environmental fate profile for ivermectin. Ivermectin is mixed with whole kernel corn and placed in feeders that are used to dispense treated corn. The potential for exposure to people is greatest for workers who mix ivermectin with the corn and fill the feeders. However, the toxicity of ivermectin to mammals, as well as label directions regarding mixing and application, suggests that the risk to this group of the population will be low. Risk to the general public will be negligible based on the method of application and program requirements that restrict access to feeders. Threats to ground and surface water that may be used as drinking water are not anticipated because of the proposed treatment method and environmental fate of ivermectin. Risk to the general public from the consumption of meat from ivermectin-treated deer will be negligible because feeding deer with ivermectin-treated corn will be discontinued 60 days prior to the deer hunting season.

The risk of ivermectin to most fish and wildlife species is expected to be very low. Ivermectin is considered toxic to aquatic organisms; however, the proposed method of application, program controls, and the environmental fate of ivermectin suggest that significant exposure to aquatic habitats will not occur. There is the possibility of exposure to some non-target terrestrial wildlife who may consume corn that is spilled onto the ground during feeding by white-tailed deer. The use of a barrier and weekly monitoring of the feeders will reduce this type of exposure to many non-target terrestrial vertebrates. The low probability of exposure and therapeutic doses of ivermectin being administered suggest that risk to non-target terrestrial vertebrates who may consume some spilled treated corn will be low. There is some risk to terrestrial invertebrates that depend on deer droppings for development. Some beetles and flies that use deer droppings for development may be impacted due to the presence of ivermectin. Impacts to this group of invertebrates will be variable based on site specific conditions that will impact ivermectin degradation and availability.

1.0 INTRODUCTION

This human health risk assessment (HHRA) and ecological risk assessment (ERA) provide a qualitative and quantitative evaluation of the potential risks and hazards to human health, non-target fish, and wildlife as a result of exposure to ivermectin. APHIS proposes the use of ivermectin-treated whole kernel corn in feeding stations to control cattle fever ticks in white-tailed deer populations.

The methods used in this HHRA to assess potential human health effects follow standard regulatory guidance and methodologies (NRC, 1983; USEPA, 2015), and generally conform to other Federal agencies such as U.S. Environmental Protection Agency, Office of Pesticide Programs (USEPA/OPP). The methods used in this ERA to assess potential ecological risk to non-target fish and wildlife follow USEPA and other published methodologies regarding eco-risk assessment, with an emphasis on those used by USEPA/OPP in the pesticide registration process.

The risk assessment is divided into four sections beginning with the problem formulation (identifying hazard), then a toxicity assessment (the dose-response assessment), and an exposure assessment (identifying potentially exposed populations and determining potential exposure pathways for these populations). In the fourth section (risk characterization) the information from the exposure and toxicity assessments are integrated to characterize risk of ivermectin use to human health and the environment.

2.0 PROBLEM FORMULATION

Cattle fever is a severe and often fatal disease of cattle transmitted by the cattle fever tick, *Rhipicephalus* (=*Boophilus*) *annulatus*, and southern cattle tick, *R. microplus*. These parasites typically attach themselves to the skin inside an animal's thigh, flanks, and forelegs or along the belly and brisket, and spread cattle fever through infected saliva. Infection can cause anemia, seizures, aggressiveness, jaundice, and death. To control cattle fever ticks, APHIS created the Cattle Fever Tick Eradication Program (CFTEP) in 1906. With the help of mounted patrol inspectors (also known as tick riders) and systematic quarantines, the CFTEP eradicated cattle fever and cattle fever tick populations from the continental United States in 1943, with the exception of a permanent quarantine "buffer" zone between Texas and Mexico. Today, this buffer zone extends over 500 miles from Del Rio, Texas, to the Gulf of Mexico (USDA APHIS, 2015).

Failure to control ticks on wildlife hosts greatly compromises efforts to eradicate ticks on livestock and poses a substantial threat of infestation and disease establishment throughout South Texas. Current efforts to control cattle fever ticks include a partial tick control barrier fence, livestock movement quarantines, population control of certain hosts such as Nilgai, and tick treatments for cattle and deer. While these methods are effective, the free-ranging movement of deer and stray livestock across non-fenced properties and an increase in the overall white-tailed deer population has recently led to increased fever tick infestations in South Texas. As of October 2009, 72 premises outside the quarantined area were found to be infested, compared to 8 infested premises in October 2006 — a nine-fold increase in 3 years (USDA APHIS, 2015).

To control ticks in deer, APHIS proposes the use of ivermectin-treated whole kernel corn bait in feeding stations as a way to deliver a systemically active acaricide. The FDA does not object to an extra-label drug use as long as all applicable provisions of 21 CFR 530 are met, which includes establishing a withdrawal period that ensures no illegal drug residues occur in treated deer (Email from Vitolis E. Vengris, Deputy Director, Division of Surveillance, Center for Veterinary Medicine, U.S. Food and Drug Administration, to Thomas R Kasari, Cattle Health Staff Veterinarian, USDA-APHIS-VS (March 14, 2016 1:00PM DST) (on file with APHIS). APHIS-VS has a 2015 agreement with the Texas Animal Health Commission and the Texas Parks and Wildlife Department on treating hosts for cattle fever ticks by feeding them with an ivermectin-treated corn product (Memorandum of Understanding between Texas Animal Health Commission (TAHC) and the Texas Parks and Wildlife Department (TPWD) and the United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) Veterinary Services (VS) (Dec. 2, 2015) on file with APHIS).

Ivermectin is a macrocyclic lactone and semisynthetic chemical derivative of avermectin that is produced by soil microorganisms (*Streptomyces avermitilis*). Ivermectin is a broad spectrum antiparasitic drug. Similar to other macrocyclic lactones, ivermectin blocks the transmission of neural signals of the parasites by binding selectively and with high affinity to the glutamate-gated chloride channels in nerve and muscle cells of invertebrates, and acting as an agonist of the gamma-aminobutyric acid (GABA) neurotransmitter in the peripheral nervous system of invertebrates and in the central nervous system (CNS) of vertebrates (Liebig, et al., 2010; Junquera, 2015; Crump and Omura, 2011). Without the transmission of neural signals, parasites are paralyzed and expelled out of the body, or starve (Junquera, 2015). In vertebrates, the GABA receptors occur only within the CNS (usually in the brain) where the blood-brain barrier prevents larger molecules, such as ivermectin, from entering the brain (Omura, 2008; Crump and Omura, 2011). As a result, ivermectin is much less toxic to vertebrates than invertebrates that lack a blood-brain barrier. This situation allows for a high safety margin when there is ivermectin use on livestock and pets against invertebrate pests.

Ivermectin is approved as a human drug under the name of Stromectol® in the United States for the treatment of strongyloidiasis and onchocerciasis (USFDA, 2016a). It is also used for the treatment of scabies, lice, and ascariasis in other countries (NIDDK, 2016). The U.S. Food and Drug Administration (FDA)-approved ivermectin human drugs currently include Stromectol® (3 milligram (mg) oral tablet), Sklice® (0.5% topical lotion), and Soolantra® (1% topical cream) (USFDA, 2016a). Ivermectin is also widely used as a veterinary medicine to treat various ecto- and endoparasites on a variety of mammals, birds, reptiles, amphibians, and fish used in agriculture, or that are held in captivity such as zoos (Panayotova-Pencheva, 2016).

2.1 Chemical Description and Product Use

Ivermectin (CAS No. 70288-86-7, $C_{48}H_{74}O_{14}$) is a mixture of mostly avermectin H_2B1a (RN 71827-03-7) with smaller quantities of avermectin H_2B1b (RN 70209-81-3), that are macrolides from the bacteria, *Streptomyces avermitilis* (NCBI, 2016) (Figure 2-1).

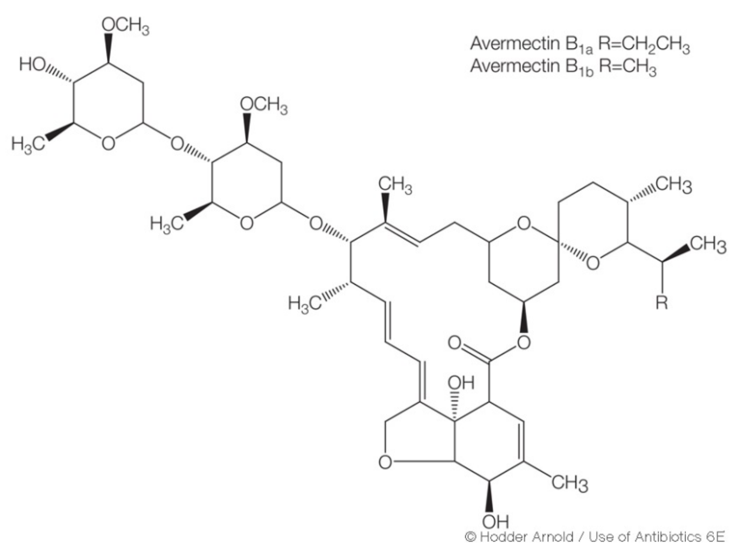

Figure 2-1. The chemical structure of ivermectin

Ivermectin is the active ingredient (a.i) in several animal medicines including the formulation Ivomec® pour-on for cattle. Ivomec® pour-on for cattle contains 5 mg ivermectin per milliliter (ml) (Merial, 2015). The formulation consists of 0.5% ivermectin compound B1a and compound B1b, 80% isopropanol, and 19.5% non-hazardous inert ingredients (Merial, 2010). Ivomec pour-on® for cattle, was originally approved by FDA (New Animal Drug Application No. 140-841) in 1990 for the treatment and control of gastrointestinal nematodes, lungworms, cattle grubs, sucking and biting lice, and sarcoptic mange mites with a supplemental approval in 1997 for persistent control of gastrointestinal roundworms. The same formulation was given a second supplemental approval in 2003 for persistent activity against *Dictyocaulus viviparus* (lungworm) for 28 days after treatment, *Cooperia surnabada* (gastrointestinal roundworm) for 14 days after treatment, and *Damalinia bovis* (lice) for 56 days after treatment. The same approval also allowed for extended persistent activity periods for *Oesophagostomum radiatum* (gastrointestinal roundworm) from 14 to 28 days after treatment and *C. punctata* and *Trichostrongylus axei* (gastrointestinal roundworms) from 14 days to 21 days after treatment. The revised labeling is to reflect updated environmental information, to speciate *Cooperia* spp. (gastrointestinal roundworms) in the treatment and control section, and to add a veal calf warning statement to the residue information section (USFDA, 2016b). Ivomec® pour-on for cattle is sold by Merial, Inc. but there is a generic product, Ivomax® pour-on for cattle (FDA ANADA 200-272), that is also available for use (Aspen, 2016). To control ticks in deer, APHIS proposes the use of ivermectin-treated whole kernel corn bait delivered to deer using a closed gravity feeding station from February through July at a rate of 10 mg of ivermectin per pound of corn.

2.2 Physical and Chemical Properties

Ivermectin is a white to yellowish-white, non-hygroscopic, crystalline powder with a molecular weight of 875 grams (g)/mole (mol) (Merck, Sharp, & Dohme Corp., 2010). It has a low vapor pressure of 1.5×10^{-9} millimeters of mercury (mm Hg) or less, suggesting it is not likely to volatilize into the atmosphere. Ivermectin has an octanol/water coefficient of 1,651 suggesting it may partition into lipids and is hydrophobic. Ivermectin is not considered soluble in water (water solubility = 4 mg/liter (L)) (Bloom and Matheson, 1993). The Ivomec® pour-on for cattle formulation is a blue liquid with an alcohol odor. It is not an oxidizing agent but is considered flammable (Merial, 2010).

2.3 Environmental Fate

The environmental fate describes the processes by which ivermectin moves and is transformed in the environment. The environmental fate processes include: 1) mobility, and migration potential to groundwater and surface water, 2) persistence and degradation, and 3) plant uptake.

Ivermectin has low volatility and is unlikely to partition into the atmosphere. Ivermectin binds strongly to soil particles based on the high soil organic carbon binding coefficients that range from 4,000 to 15,700 L/kilogram (kg) (Halley et al., 1989a; Liebig et al., 2010). Variations in soil binding coefficients are due to the various soil types and organic carbon concentrations tested in each soil. The strong binding affinity of ivermectin to soil and sediment means it is unlikely to leach into groundwater or runoff to surface water in a dissolved state. Ivermectin was not detected in leachate in a leaching study with soils containing 2.3 and 6.3% organic carbon content (Oppel et al., 2004). Halley et al. (1989a) reported 39% to 45% of the applied radioactivity remained in the top 5 centimeters (cm) of the soil column, and 10% to 48% leached as metabolites or degradation products. No ivermectin parent material was detected in the leachate.

Table 2-1. Environmental fate half-lives for ivermectin.

Compartment	Half-life (days)	Reference
Water (dissipation)	<0.25-5	Prasse et al., 2009; Loffler et al., 2005; Sanderson et al. 2007
Water (degradation)	<1-30	Bloom and Matheson, 1993; Liebig et al., 2010
Water/sediment (dissipation)	15-130	Prasse et al., 2009; Loffler et al., 2005; Liebig et al., 2010
Sediment (degradation)	130	Liebig et al., 2010
Soil (dissipation)	16.1-36.1	Krogh et al., 2009
Soil (degradation)	7-217	Halley et al., 1989a

Ivermectin breaks down to less bioactive compounds via photo and aerobic degradation (Halley et al., 1993). Degradation of ivermectin in soil depends on the soil type and properties, sorption capacity, as well as temperature (Krogh et al., 2009). Ivermectin half-lives in soil are 7 to 14 days at high temperatures in summer, but can be much longer (91 to 217 days) at low temperatures in the winter (Bloom and Matheson, 1993; Halley et al., 1993). Photolysis of ivermectin in water is less than 0.5 day in summer and 39 hours in winter (Halley et al., 1993; Bloom and Matheson, 1993). Its photolytic half-life was approximately 3 hours on a thin, dry film exposed to direct sunlight (Halley et al., 1989a).

Studies in cotton and food crops (sorghum, lettuce, carrots, and turnips) show that plants uptake little ivermectin from direct applications to plants or from soil (Merck & Co., Inc., 1991). Greenhouse and field trial studies were performed in seventeen terrestrial species by exposing the plants to high levels of several ivermectin analogs. The studies did not show phytotoxic effects at foliar application rates as high as 10 kg/hectare (ha) of ivermectin-like material. The study results also indicated that ivermectin analogs are not readily translated into plants from the soil or from directly spraying (Bloom and Matheson, 1993).

2.4 Hazard Identification for Human Health

FDA has approved ivermectin for human use; however, it can be a hazard to human health in accidental intoxication or when significant exposures to veterinary formulations occur. The most frequently reported adverse effects include rash, edema, headache, dizziness, asthenia, nausea, vomiting, and diarrhea (Merck, Sharp, & Dohme Corp., 2010). The Ivomec® pour-on for cattle formulation has a narcotizing effect and is irritating to eyes. Vapors of the formulation may cause drowsiness and dizziness (Merial, 2010). Symptoms from overexposure to the Ivomax® pour-on for cattle formulation may include decreased activity, slow rate of breathing, dilation of the pupils, muscle tremors, and in-coordination (Aspen, 2013). The Ivomax® pour-on formulation can cause eye irritation from direct eye contact, and may cause irritation and/or drying and cracking of the skin from prolonged or repeated contact.

2.4.1 Toxic Effects

Acting as a GABA agonist, ivermectin has reduced toxicity in mammals and other vertebrates compared to invertebrates because GABA is found only in the CNS of mammals and is normally protected by the blood-brain barrier. In humans, the symptoms of toxic effects from overdose exposure to ivermectin include rash, edema, headache, dizziness, asthenia, nausea, vomiting, and diarrhea. Other symptoms include seizure, ataxia, dyspnea, abdominal pain, paresthesia, and urticarial and contact dermatitis (Merck, Sharp, & Dohme Corp., 2010).

Higher ivermectin toxic effects are reported in some dog breeds such as collies, Shetland sheepdogs, old English sheepdogs, Australian collies, and their crosses. These breeds are more sensitive to ivermectin due to a mutation of the multiple drug resistance gene (MDR1) causing an abnormality in the blood-brain barrier and allowing increased ivermectin into the CNS. The symptoms include mydriasis, ataxia, and tremors, as well as collapse, coma, and respiratory collapse at higher doses (Merck, Sharp, & Dohme Corp., 2016).

Some dogs are homozygous for a mutation to produce a severely truncated P-glycoprotein (<10% of the normal amino acid sequence). Dogs with this mutation will develop ivermectin toxicity at any of the dosages used to treat demodicosis. Idiosyncratic reactions may develop in any breed (Merck, Sharp, & Dohme Corp., 2016).

2.4.2 Metabolism

Ivermectin is absorbed into blood, distributed throughout the mammal's body (Canga et al., 2009). Ivermectin tends to be deposited in the body fat and the liver, where it is progressively metabolized (biotransformation) and excreted. Main factors affecting absorption are route of administration, formulation, and animal species. Compared to monogastric animals, the ruminant species appear to have a slower absorption process after oral administration, and a longer plasma elimination half-life after intravenous administration (Canga et al., 2009). Animal studies show approximately 90% of the dose administered parenterally or orally is excreted in the feces with unchanged parent compound in tissue residues (Canga et al., 2009, Campbell, 1985). Only 0.5 to 2% of the dose is excreted in urine (Campbell et al., 1983), and less than 1% appeared in the urine and less than 2% in breast milk (Temple and Smith, 1992). Approximately half (39-45%) of the ivermectin in feces of subcutaneously treated cattle are the parent compound and 54% are polar metabolites (Halley et al., 1989). In humans, ivermectin is primarily metabolized in the liver by cytochrome P450 enzymes (Canga et al., 2008).

2.4.3 Human Case Study

Guzzo et al. (2002) performed a dose escalation study in humans to evaluate ivermectin CNS effects and general toxicity of ivermectin. Sixty-eight healthy adults were administered in higher and/or more frequent doses (three times a week of 30 or 60 mg, or single dose of 90 or 120 mg) than the approved dose for human use. Mydriasis quantitated by pupillometry was the primary safety endpoint. The study showed that ivermectin is generally well tolerated by healthy adults, with no indication of associated CNS toxicity at levels up to 10 times the highest FDA-approved dose of 200 µg/kg.

Approximately 40 cases of self-injection with ivermectin solutions intended for animal use reported the major effect as pain at the injection site. Other reported effects include nausea, paresthesia, variable blood pressure, urticaria, and cellulitis. Dermatitis was the main reaction following dermal exposure. Approximately 10 cases of accidental ingestion of ivermectin solution or tablets by adults reported adverse effects of mydriasis, vomiting, tachycardia, and somnolence (Woodward, 2016).

An acute liver injury was reported from a single dose of ivermectin (15 mg orally) used as a subsequent treatment for low levels of microfilariae in the blood in a 20 year old woman from Cameroon (NIDDK, 2016; Veit et al., 2006). The patient developed hepatitis and experienced abdominal pain and elevated serum aminotransferase levels one month after treatment. A liver biopsy showed intralobular inflammatory infiltrates, confluent necrosis, and apoptosis compatible with drug-induced liver disease. Symptoms improved and serum aminotransferase levels fell rapidly within days and the patient fully recovered four months later.

2.4.4 Acute Toxicity

The acute oral LD_{50s} are 25 mg/kg in mice and 50 mg/kg in rat. The acute dermal LD_{50s} are higher than 660 mg/kg in rats and 406 mg/kg in rabbits. The acute oral LD_{50} in dogs without the MDR1 gene defect is 80 mg/kg. The acute oral LD_{50} for rhesus monkey is >24 mg/kg (Lankas and Gordon, 1989). The acute oral LD_{50} for dogs with the MDR1 gene defect is 0.2 mg/kg (Hopper et al., 2002).

The safety data sheet for the formulation reports oral LD_{50} values for ivermectin comp. B1a and comp. B1b are greater than 15 mg/kg (adult human), ~80 mg/kg (dog), 25 mg/kg (mouse), 50 mg/kg (rat), and higher than 24 mg/kg (rhesus monkey). The dermal LD_{50s} are 406 mg/kg (rabbit) and >660 mg/kg (rat). Inhalation LC_{50} values are 0.4 mg/kg (rat) and 1.6 mg/kg (adult human). The intraperitoneal LD_{50} is 55 mg/kg (rat), and the subcutaneous LD_{50} is ~10 mg/kg (juvenile dog) (Merial, 2010).

2.4.5 Subchronic and Chronic Toxicity

A 3-month oral toxicity study in rats exposed to ivermectin via *in utero* at dose levels of 0.4, 0.8, and 1.6 mg/kg/day reported a no observable effect level (NOEL) of 0.4 mg/kg/day. At 0.8 mg/kg/day and above, splenic enlargement and reactive hyperplasia of the bone marrow were observed (Lankas and Gordan, 1989).

A 3-month oral toxicity study in beagle dogs exposed to ivermectin via gavage at dose levels of 0.5, 1.0, and 2.0 mg/kg/day reported a NOEL of 0.5 mg/kg-day. Mydriasis was observed at 1.0 mg/kg/day. Tremors, ataxia, and anorexia were observed at 2.0 mg/kg/day (Lankas and Gordan, 1989).

A 16-day oral toxicity study in immature rhesus monkey exposed to ivermectin via nasogastric intubation at dose levels of 0.3, 0.6, and 1.2 mg/kg/day reported a NOEL of >1.2 mg/kg/day with no treatment-related effects (Lankas and Gordan, 1989).

2.4.6 Nervous System Effects

CNS effects and visual disturbances have been observed at relatively high doses in mammals. Some mammals such as rodents are more sensitive to ivermectin CNS effects than others such as primates. Rats administered ivermectin intravenously at 4 mg/kg, produced moderate incoordination. A dose of 6 mg/kg induced a state resembling anaesthesia (started one minute after injection and lasted for four to five hours). Higher doses caused respiratory depression and resulted in death (Hayes and Laws, 1991).

A 14-week oral toxicity study in dogs reported no treatment-related effects in dogs given 0.5 mg/kg/day. Dogs given 1 mg/kg/day developed mydriasis and lost a small amount of weight. Dogs given 2 mg/kg/day developed tremors, ataxia, anorexia, and became dehydrated (Temple and Smith, 1992).

Campbell and Benz (1984) reported ataxia with tremors in dogs given oral doses of 10 mg/kg ivermectin. Death occurred at 40 mg/kg due to respiratory depression. Collie dogs have been shown to be more sensitive than other dogs to the toxic effects of ivermectin. Depression, tremors, mydriasis, ataxia, coma, and death have been seen in collie dogs at 100 µg/kg orally and greater, but not at the recommended dose of the commercial product (6 ug/kg) (Campbell and Benz, 1984; Hopper et al., 2002).

2.4.7 Reproductive or Developmental Effects

Lankas and Gordon (1989) reported ivermectin's toxic effects in a reproductive and neonatal toxicity study in several generations of rats. The study results showed ivermectin (oral administered dose as low as 0.4 mg/kg body weight per day) caused increased postnatal pup mortality and a decrease in pup body weight in survival offspring. Neonatal rats are more sensitive to ivermectin because they form the blood-brain barrier during the postnatal period. Other mammals such as humans, sheep, and rabbits form the blood-brain barrier during the prenatal period.

A 3-year study in Liberia identified 203 children born to women inadvertently treated with ivermectin during pregnancy. There was no increased incidence of birth defects in these children, when compared with children born to untreated mothers in the same population or in a reference population (Pacque, et al., 1990).

2.4.8 Carcinogenicity and Mutagenicity

A one-year carcinogenic study using male Wistar rats (0 and 2 parts per million (ppm) of ivermectin in diet) reported negative results (O'Connor et al., 2001). Ivermectin is not listed as carcinogenic by the U.S. National Toxicology Program or the International Agency for Research on Cancer.

Mutagenicity studies (the AMES Assay and a mouse lymphoma mutation assay) with ivermectin have been negative. Ivermectin did not induce unscheduled DNA synthesis in a human fibroblast cell culture or damage DNA (Temple and Smith, 1992).

2.4.9 Endocrine System Effects

The available data does not indicate ivermectin has endocrine system effects.

2.4.10 Immune System Effects

The available data does not indicate ivermectin has immune system effects. An ivermectin immune study in rabbits and rats did not show direct immune response (Uhlir and Volf, 1992).

2.4.11 Toxicity of Other Ingredients

The Merial safety data sheet lists 80% of the Ivomec® pour-on for cattle formulation as isopropanol (CAS # 67-63-0), 19.5% non-hazardous inert ingredients and the remaining 0.5% as ivermectin (Merial, 2010). More than 60% of the Ivomax® pour-on for cattle formulation is isopropanol (Aspen, 2013). Isopropanol has low toxicity (Category III) in oral dosing and very low toxicity (Category IV) in dermal and inhalation exposures. The oral LD_{50} in rats is 4,570 mg/kg. The dermal LD_{50} in rabbits is 13,400 mg/kg and the inhalation LC_{50} in rats is 30 mg/L (Merial, 2010). Ingestion of a large amount of isopropyl alcohol will cause burning of the gastrointestinal tract, nausea, vomiting, and CNS depression (Aspen, 2013).

3.0 DOSE-RESPONSE ASSESSMENT

3.1 Human Health Dose-Response Assessment

A dose-response assessment evaluates the dose levels (toxicity criteria) for potential human health effects including acute and chronic toxicity.

The FDA has established tolerances for the proposed ivermectin formulation in the CFTEP. For 22,23-dihydroavermectin B1a (marker residue) in liver (target tissue), the tolerances are 1.6 ppm in cattle, 20 parts per billion (ppb) in swine, 30 ppb in sheep, and 15 ppb in reindeer and American bison. Muscle residues are not indicative of the safety of other edible tissues. For 22,23-dihydroavermectin B1a (marker residue) in muscle, the tolerances established include 20 ppb for swine, and 0.65 ppm for cattle (USFDA, 2016c).

3.2 Ecological Dose-Response Assessment

3.2.1 Wild Mammal, Avian and Reptile Toxicity

Ivermectin has been used as a treatment for internal and external parasites in various mammals, birds and reptiles (Panayotova-Pencheva, 2016). The toxicity of ivermectin to mammals is characterized in the above human health section that covers acute and chronic effects in laboratory animal studies. Acute oral toxicity values range from 25 to approximately 80 mg/kg, suggesting ivermectin is moderately to slightly toxic to mammals.

Acute toxicity of ivermectin to birds is considered low to moderate depending on the test species. The oral LD_{50} for ivermectin to bobwhite quail is 2,000 mg/kg and 88 mg/kg for the mallard duck. Similar sensitivities are seen in dietary studies with LC_{50} values of 3,102 and 383 mg/kg, for the bobwhite quail and mallard, respectively (Bloom and Matheson, 1993). Little toxicity data appears to be available for reptiles; however, tortoises have been reported as less tolerant of therapeutic doses of ivermectin than other terrestrial vertebrates (Halley et al., 1989b). These studies appear to be based on injected doses of ivermectin in reptiles, thus the applicability to this risk assessment is limited because the primary route of exposure would be from the consumption of ivermectin-treated corn. USEPA/OPP uses avian data as a surrogate to represent the sensitivity of reptiles to pesticides. There is uncertainty in that assumption however. With the lack of oral dosing toxicity data for reptiles, ivermectin is considered low to moderately toxic to reptiles.

3.2.2 Terrestrial Invertebrate Toxicity

Terrestrial invertebrate toxicity data for ivermectin is primarily related to soil dwelling and dung dependent invertebrates because of the method of application for most ivermectin uses, and residues that may occur in droppings or manure from treated animals. Jensen et al. (2003) reported EC_{50} values and no observable effect concentrations (NOEC) of 1.7 and 0.3 mg/kg dry soil for collembolans, and 36 and 3 mg/kg for enchytraeids, respectively, in 21-day exposures. Forster et al. (2011) evaluated the impacts of ivermectin on a variety of soil borne invertebrates from field collected soil that was dosed at various ivermectin levels and found collembolans to be the most sensitive taxa. Rombke et al. (2010a) showed similar results when comparing lethal and sublethal effect levels in laboratory exposures using the collembolan, *Folsomia candida*, earthworm, *Eisenia fetida*, and predatory mite, *Hypoaspis aculeifer*. The EC_{50} and NOEC for the collembolan, earthworm, and predatory mite were 1.7 and 0.3, 5.3 and 2.5, and 17.8 and 3.2 mg/kg dry soil, respectively. The toxicity values estimated for the earthworm are some of the lower reported values and may be due to differences in organic carbon content in the test soils between studies which can alter the bioavailability of ivermectin.

Invertebrates in the Diptera and Coleoptera insect orders are the primary taxa with species that are dependent on dung for development. Work evaluating invertebrate colonization of cattle dung containing ivermectin has shown negative effects to various insect taxa and impacts to species diversity (Suarez et al., 2003; Jochman et al., 2015). The range of doses and effects that cause adverse effects are variable and depend on the type of formulation being tested, dosing method used, species dosed, and environmental variables in fields where the studies were conducted (Wall and Beynon, 2012). Blackenhorn et al. (2013) evaluated the effects of ivermectin on 21 species of sepsid dung and black scavenger flies and found a wide range of sensitivities. Lethality values (LC_{50}) ranged from 0.05 to 18.55 micrograms (µg) ivermectin/kg dung. Larval Diptera and Coleoptera are the life stage most affected by ivermectin, and cyclorrhaphous dipteran larvae are more sensitive than coleopteran larvae (Rombke et al., 2010b; Steel and Wardhaugh, 2002). The impact to invertebrates from ivermectin has shown mixed effects regarding whether there are impacts to dung degradation which could impact nutrient cycling (Floate et al., 2005).

3.2.3 Terrestrial Plant Toxicity

No terrestrial phytoxicity data appears to be available for ivermectin. However, studies using analogs of ivermectin have shown low phytotoxicity when applied directly to plants at levels up to 10 kg/ha (Bloom and Matheson, 1993). Ivermectin that may occur in soil or manure, or applied directly to plants will not translocate and result in adverse effects to terrestrial plants.

3.2.4 Aquatic Toxicity

Ivermectin is considered highly toxic to most aquatic invertebrates based on available laboratory and field toxicity studies. Acute toxicity values range from 25 nanograms (ng)/L to 400 µg/L with cladocerans being the most sensitive aquatic invertebrate species (Table 3-1). The sensitivity of cladocerans to ivermectin has also been confirmed in mesocosm studies showing acute impacts to cladoceran populations at 30 ng/L. Other invertebrates such as ostracods, copepods, and ephemeropterans were less sensitive in acute exposures with predicted NOECs ranging from 100 to 1,000 ng/L (Sanderson et al., 2007). Chronic toxicity to aquatic invertebrates is also high. Lopes et al. (2009) reported NOECs of 0.0003 and 0.001 ng/L for the freshwater cladocerans, *Daphnia magna* and *Ceriodaphnia dubia*, respectively. Garric et al. (2007) also reported a NOEC of 0.0003 ng/L for *D. magna* in 21-day exposures that assessed impacts on reproduction and growth. Aquatic invertebrate toxicity from ivermectin can be ameliorated due to the partitioning of ivermectin in the presence of organic material. Carbonell-Martin et al. (2011) report a 48-hour EC_{50} of 0.50 µg/L for *D. magna* in soil leachate which is an approximate 10-100 fold reduction in toxicity compared to values reported in water without organic matter. Two of the primary hydrolytic metabolites of ivermectin have been shown to be between 16 and >680 times less toxic to *D. magna* than the parent material (Halley et al., 1989b).

Table 3-1. Acute toxicity of ivermectin to freshwater and marine invertebrates.

Species	EC/LC$_{50}$	Reference
Daphnia magna, cladoceran	5-25 ng/L	Garric et al., 2007; Halley et al., 1989b
D. similis	70 ng/L	Dal Basco et al., 2011
Neomysis integer, mysid shrimp	70 ng/L	Davies et al., 1997
Gammarus pulex, freshwater amphipod	1.8-2.1 µg/L*	Alonso et al., 2010
G. fusarium	2.1-3.6 µg/L*	Alonso et al., 2010
Mytilus edulis, Eastern oyster	400 µg/L	Davies et al., 1997
Tubifex tubifex, oligochaete	2.0 mg/L	Gerhardt, 2009

*value approximated from graph for adults and juveniles

Effects to benthic inverterbrates have also been evaluated for various species due to the low solubility of ivermectin and its preferential binding to soil and sediment. Egeler et al. (2010) reported 28-day EC$_{50}$ values for the chironomid, *Chironomus riparius*, ranging from 9.0 to 64 µg/kg and NOECs ranging from 3.1 to 25 µg/kg, depending on the endpoint. The most sensitive NOEC was based on statistical differences in individual dry weight. The oligochaete, *Lumbriculus variegatus*, was less sensitive compared to *C. riparius* in a similar 28-day exposure with an EC$_{50}$ value of 2,980 µg /kg and NOEC of 160 µg/kg based on the total number of worms. Allen et al. (2007) evaluated the impacts of sediment-bound ivermectin to the marine amphipod, *Corophium volutator* and polychaete, *Arenicola marina* in 10-day exposures. The lowest LC$_{50}$ and NOEC values were reported as 14.8 and 2.0 µg/kg for the amphipod, and an LC$_{50}$ of 21.9 for *A. marina*. Brinke et al. (2010) reported NOECs of 0.62 and 0.06 µg/kg for meiobenthic and nematode communities, respectively, in ivermectin-dosed sediments in freshwater mesocosms.

Ivermectin is used as a therapeutic treatment for fish and amphibians. The toxicity of ivermectin to aquatic vertebrates is much less when compared to aquatic invertebrates with 96-hour LC$_{50}$ values ranging from 3.3 to 5.3 µg/L, for the rainbow trout, *Onchorynchus mykiss*, and bluegill sunfish, (*Lepomis microchirus*) respectively (Halley et al., 1989b). The acute NOEC in the rainbow trout study was reported as 0.9 µg /L. The sea bream, *Sparus aurata*, is less sensitive than the bluegill sunfish and rainbow trout with no mortalities reported in 96-hour exposures between 0.056 and 0.32 mg/L (Mladineo et al., 2006). The 96-hr LC$_{50}$ for the Atlantic salmon, *Salmo salar*, is reported as 0.017 mg/L (Kilmartin et al., 1996). The zebrafish, *Danio rerio*, has comparatively lower sensitivity to ivermectin with a 144-hour LC$_{50}$ value of 0.44 mg/L and a NOEC of 0.22 mg/L (Carlsson et al., 2013). Ivermectin sensitivity for amphibians appears to be in the range of sensitivities for fish based on one 96-hour LC$_{50}$ value of 5.5 µg/L, with a NOEC of 1.1 µg/L, for the African clawed frog (*Xenopus laevis*) (Martini et al., 2012).

Ivermectin has low toxicity to aquatic plants with no impacts noted for green algae, *Chlorella pyrenoidesa*, in a 14-day exposure at concentrations up to 9.1 mg/L (Halley et al., 1989b).

4.0 EXPOSURE ASSESSMENT

4.1 Human Health Exposure Assessment

The exposure assessment estimates the potential exposure of humans to ivermectin. The exposure assessment begins with the use and application method for ivermectin in the CFTEP. A complete exposure pathway for ivermectin includes (1) a release from an ivermectin source, (2) an exposure point where contact can occur, and (3) an exposure route such as ingestion, inhalation, or dermal contact by which contact can occur. In this way, the potentially exposed human population and complete exposure pathways are identified. Finally, exposures for the identified human populations are qualitatively evaluated for each exposure pathway.

APHIS uses the Ivomec® or Ivomax® pour-on for cattle formulation mixed with whole kernel corn that is placed in gravity flow feeding stations from February through July to control cattle fever ticks in deer populations. The gravity flow feeder is a commercially made plastic bin device with four feed tubes below the bin, and a lid (Figure 4-1). Each feeder has a holding capacity of approximately 300-350 pounds of corn. Each feed site will include one gravity flow feeder. Feeders will be enclosed with welded wire panels to exclude non-target animals (such as hogs, javelina, or livestock). The feeders will be serviced and filled weekly. The program office will maintain records including wildlife treatment feeding/bait station data sheets, service record sheets, and a map showing the number and location of each feeding station (USDA APHIS, 2016).

Figure 4-1. Closed gravity feeder system used to dispense ivermectin-treated corn to white-tailed deer.

For dosing, 200 ml of the formulation containing 5 mg ivermectin/ml will be pumped into one hundred pounds of clean corn to produce 10 mg of ivermectin a.i. per pound of corn. The feeding rate for deer is approximately 1% of body weight per day or approximately 1 pound per 100 pound deer per day. The daily intake dose of the deer is approximately 0.22 mg/kg assuming a 100 pound white-tailed deer eats 1 pound of corn per day. A previous study concluded that a feeding rate of 0.22 mg/kg should produce maximum blood serum levels of approximately 30 ppb (Pound et al., 1996). The target concentration of 30 ppb assures a high degree of efficacy even in those deer that may consume as little as one-third of the targeted dosage. The serum levels of 10 ppb should produce 100% efficacy against ticks attempting to feed on treated animals (Pound et al., 1996; Nolan et al., 1985; Miller et al., 1989). The ivermectin-treated corn will be fed to white-tailed deer throughout the treatment period (February through July).

The number of feed sites will be determined based on number and density of deer (1 feeder per 20-30 deer to minimize excessive competition and social dominance), and density of feeders per area (deer do not have to travel more than 1/4 to 1/2 mile to access feed= 1 per 125 acres to 1 per 500 acres).

Based on the application method, workers in the program are the most likely human population segment to be exposed to ivermectin. Occupational exposure to ivermectin may occur through incidental ingestion, inhalation, and dermal contact during application (mixing the formulation with corn and loading it into the feeding station). However, direct contact to ivermectin during outdoor application is not expected to occur under normal conditions with proper worker hygiene and properly functioning personal protective equipment (PPE). The safety data sheet states to use the product only in well ventilated areas, and use a suitable respiratory protective device when aerosol or mist is formed (Merial, 2010). The PPE for program workers applying the material to whole kernel corn baits includes vinyl, nitrile, or rubber gloves, a waterproof bib-apron, and suitable eye protection (Merial, 2010; Aspen, 2013). Accidental exposure may occur during mixing of ivermectin with corn from liquid splashing or otherwise being transferred from contaminated gloves or clothing to an unprotected skin area (usually the face). However, these types of accidental exposures are unlikely with well-trained applicators. Drift from the application will not occur because baits are placed directly into the gravity feeding stations.

A complete exposure pathway associated with direct contact to ivermectin from the proposed application method is unlikely for the general public because they will have restricted access to the feeding stations. A lock will be installed at points of access to the property to allow systematic access to the premises/feeders (USDA APHIS, 2016). Comparable security will be provided at refuges and other public sites. Based on the APHIS feeding station use pattern, the potential for the general public to be exposed to ivermectin is not expected via inhalation, dermal exposure, or through ingestion of treated corn.

A complete exposure pathway is not identified for dietary consumption of deer meat from the treated deer because the APHIS program requires no less than 60 days of withdrawal time before the start of the hunting season (USDA APHIS, 2016). FDA does not have an established withdrawal time for white-tailed deer. The FDA established a withdrawal time for reindeer of 56 days based on a subcutaneous dose of 10 mg per 50 kg body weight and a liver (target tissue) tolerance of 15 ppb (USFDA, 2016d; 21 CFR 522.1192; Dieterich and Craigmill, 1990). Based on available data, the residual ivermectin serum and tissue concentrations in white-tailed deer should decrease to non-detectable levels and less than the tolerance level of 15 ppb, respectively before the withdrawal time of 60 days. Mackintosh et al. (1985) reported the elimination half-life of 6 days in the blood plasma of red deer calves after a subcutaneous administration of ivermectin at 0.2 mg/kg. The half-lives in tissue after a single subcutaneous treatment of ivermectin at 0.2 mg/kg were 7.1 days in back fat, 2.9 days for the injection site, 4.9 days for muscle, 5.8 days for liver, and 5.7 days for kidney (EMEA, 2004). A withdrawal time of 60 days (10x the elimination half-life of 6 days) was estimated based on the extra label use in food animals (Riviere et al., 1998; Baynes et al., 2000). The use of 10x the elimination half-life is a conservative approach that will insure eliminate 99.9% of the drug (Riviere et al., 1998). The ratio of 22,23-dihydroavermectin B1a in tissues at 28 days following a single percutaneous administered dose of 1 mg/kg to red deer was 6.8:2.5:1.3:1 for fat, liver, kidney and muscle. The mean concentrations of 22,23-dihydroavermectin B1a in fat, liver, muscle, and kidney at 28 days after treatment were 13.2, 9.3, 1.4, and 3.6 µg/kg, respectively. The ratio of 22,23-dihydroavermectin B1a in tissues at 17 days after a single subcutaneous dose of 0.2 mg ivermectin/kg in reindeer was 9.5:6.6:2.6:1 in fat, liver, kidney and muscle, respectively (EMEA, 2004). A study using penned female and male white-tailed deer administered by direct subcutaneous ivermectin injection or ingesting ivermectin-treated whole corn, showed ivermectin serum concentrations decreased below detectable levels (<2 ppb) within 21 days after injection and 14 days after ingestion (Pound et al., 2004). The potential exposure to ivermectin residues higher than the tolerance level from consumption of deer meat treated with ivermectin-corn for the general public is precluded by cessation of feeding of ivermectin-treated corn to allow a withdrawal period of 60 days before the start of the hunting season.

A complete exposure pathway is not identified for the groundwater medium. Small amounts of ivermectin may be released to the soil in deer droppings; however, ivermectin soil concentrations would be extremely low due to the small amounts of droppings and ivermectin degradation and low solubility. In addition, any parent material would bind to soil and be unavailable to leach into groundwater (see Section 2.3).

A complete exposure pathway is not identified for the surface water medium. Significant surface runoff of ivermectin is not expected to occur from the use of treated corn. Feeding stations are placed a minimum of 50 feet from any aquatic areas and it is unlikely that any treated corn would be transported during a rain event to any surface water source used for drinking water. Any ivermectin transported to surface water would degrade and/or partition into sediment.

4.2 Ecological Exposure Assessment

4.2.1 Terrestrial Exposure Assessment

Exposure of ivermectin-treated corn to terrestrial non-target organisms will be minimized by the use of a closed gravity system feeder designed to be accessed by white-tailed deer through four spouts (Figure 4-1). Each spout has a baffle which can be adjusted to minimize spillage during feeding. Panels that are 34 inches high by 16 feet long are placed in a 15-foot radius around the feeder to reduce access by non-target wildlife and domestic animals. Long-term exposure will also be minimized by placement of the feeders in target areas from February to July.

Although the amount of spillage from the feeders is expected to be minimal (<5%), the spilled treated corn would be consumed by white tailed deer, or could be consumed by nontarget animals that are able to get within the panels. Expected ivermectin residues in corn are 22 ppm based on the mixing instructions to ensure white-tailed deer receive an effective dose.

In addition to the exposure of non-target animals to ivermectin-treated corn, the metabolism of ivermectin in mammals suggests that some of the chemical will be present in feces from the target organism, as well as any non-target organisms that may feed on the treated corn that is spilled on the ground. This type of exposure would be greatest for soil-borne invertebrates and those invertebrates that depend on deer droppings for development. Exposure will decrease over time due to environmental degradation of ivermectin in feces and soil.

4.2.2 Aquatic Exposure Assessment

The potential for exposure to aquatic organisms from ivermectin-treated corn is expected to be negligible. Ivermectin is mixed with whole kernel corn and dispensed from a closed gravity feeder system to deer (Figure 4-1). Drift of ivermectin to aquatic areas is not anticipated based on the use pattern. Runoff would also not be anticipated because the corn is contained within a feeder that is accessed by deer. There is the possibility of some spillage from deer feeding at the feeders although the amount of corn would be minor because that corn would likely be consumed by deer or other non-target organisms. Previous studies to evaluate ivermectin effectiveness in controlling ticks in white-tail deer populations have shown that little to no treated corn is available on the ground (Pound et al., 1996; Rand et al., 2000). Any corn left on the ground would not be expected to runoff into aquatic areas due to the size of the kernels with a very low probability of movement in a rain event. Ivermectin has low water solubility and partitions strongly to soil and organic matter and would not be expected to be in solution in detectable levels if there was a rain event that could result in transport of treated corn into aquatic habitats. The program does not place feeders within 50 feet of aquatic habitats, further reducing the probability of any aquatic exposure. Deer droppings containing ivermectin may be transported as runoff or deposited directly into aquatic habitats but this is not expected to be a major pathway of exposure for most aquatic organisms. Ivermectin in deer droppings would be bound to organic matter and not available to most aquatic organisms. Sediment dwelling invertebrates could be exposed due to the preferential binding of ivermectin to organic matter. However, the low probability of significant quantities of deer droppings being deposited into aquatic habitats, and the degradation of ivermectin would suggest that exposure to benthic aquatic invertebrate populations would be negligible.

5.0 RISK CHARACTERIZATION

5.1 Human Health

The use of ivermectin-treated corn in feeding stations to control cattle fever ticks is expected to pose minimal risks to human health under the APHIS proposed applications.

The greatest risk to human health is to workers who mix the ivermectin with the corn and those workers who fill the feeders. The risk to these types of workers from ivermectin via oral, inhalation, and dermal exposure is minimized by adherence to the proper use of PPE. Although ivermectin is a hazard to humans at high doses, the low potential for exposure to ivermectin from the bait application suggests that adverse effects to workers will not occur. Accidental exposure may occur from splash to unprotected body areas during mixing of ivermectin with corn. The exposure frequency would be low following the label safety precautions; therefore, risk from accidental exposure is minimal.

The risk to the general public from exposure to ivermectin-treated corn from the feeders is expected to be negligible. The feeders are placed on properties that will have a point of access that will be locked. Feeders are checked weekly so that those that are damaged will be repaired or removed, reducing the potential for exposure to the public from corn that may spill out onto the ground if the feeder is damaged. Risk to the public from the consumption of harvested white-tailed deer will also be negligible because the ivermectin-treated corn is removed from the feeder 60 days prior to the hunting season to allow ivermectin residues to decrease to non-detectable levels in white-tailed deer.

5.2 Terrestrial and aquatic risk characterization

Direct risk to non-target mammals, birds, and reptiles is expected to be low based on the method of application for ivermectin-treated corn and toxicity of ivermectin to birds, reptiles, and mammals. The use of the closed gravity feeder will reduce risk to most non-target birds, reptiles, and mammals. In addition, the use of panels surrounding the feeders will further prevent access for many terrestrial non-target organisms and exposure to any corn that may spill from the baffles during feeding. Feeders are checked weekly by program staff and adjusted to reduce corn from spilling onto the ground during feeding which could then be consumed by non-target vertebrates. The available toxicity profile for terrestrial vertebrates and dosing levels for white-tailed deer suggest that non-target domestic and wildlife vertebrate species would have to ingest more than their typical daily consumption rates to reach a dose that could result in adverse effects.

The risk to non-target birds and mammals that could enter the enclosures and consume any ivermectin-treated corn left on the ground was estimated using the bobwhite quail, mallard, and deer mouse because toxicity data is available for all three species. Doses for species were estimated using average body weights and daily food consumption rates reported by EPA (USEPA, 1993). The concentration of ivermectin in treated corn was assumed to be 22 ppm based on the target concentration needed for effective tick control for white-tailed deer. Using the body weight, daily food consumption rates, and ivermectin residues, a daily dose of ivermectin for each species could be calculated and then compared to the available toxicity data to determine whether consumption of ivermectin-treated corn would exceed effect levels. The assumption was that both non-target species would consume ivermectin-treated corn and would not consume any other food material.

Table 5.1. Estimates of exposure and risk to non-target bird and mammal species from ivermectin-treated corn.

Test Species	Body Weight (g)	Food Ingestion Rate (g/g-day)	Ivermectin consumed (mg ivermectin/animal)	Ivermectin Dose (mg/kg)	LD_{50} (mg/kg)
Bobwhite quail	154	0.067	0.23	1.49	2000
Mallard	1134	0.055	1.38	1.21	88
Deer Mouse	21	0.415	0.19	9.05	25

Based on the estimates of ivermectin doses calculated for both species the bobwhite quail would have to consume approximately 1,342 times its daily food consumption rate to exceed the median lethality value. The mallard would have to consume 73 times its daily consumption rate to exceed its medial lethality value. The deer mouse would have to consume approximately 2.7 times its daily food consumption rate to exceed the median lethality value. These estimates suggest that the acute risk to small non-target birds and mammals that consume ivermectin-treated corn would be low. No toxicity data is available for reptiles; however, assuming that the avian effects data is comparable would suggest that any reptiles that consume ivermectin-treated corn would be at low acute risk. The risk to listed birds, such as the whooping crane would also be low based on the above estimates of risk for the mallard and bobwhite and food preference. Whooping crane diet in southern Texas consists primarily of blue crabs, clams, snails, wolfberry fruit, acorns and crayfish (Hunt and Slack, 1989). The risk to aquatic food items from the use of ivermectin-treated corn is low based on the use pattern for ivermectin and the use of an application buffer from aquatic areas that will reduce the risk to aquatic organisms that may serve as a food source for the whooping crane. Risks to the wolfberry fruit and oak species from ivermectin-treated corn are negligible due to the method of application and the low toxicity of ivermectin analogs to terrestrial plants. Whooping cranes may also consume waste corn from fields so there is a possibility that they could enter enclosures and feed on spilled corn from the feeders. The low risk to other avian species such as the bobwhite and mallard suggests that the whooping crane would have to consume many times its daily food consumption rate of ivermectin-treated corn to exceed an effect threshold.

Risk to vertebrate scavengers and predators that may consume white-tailed deer that have ingested ivermectin-treated corn would be expected to be low because the ivermectin dose being delivered is therapeutic. In addition, white-tailed deer are only receiving ivermectin-treated corn February through July and would have reduced levels immediately after feeding for 60 days with no detectable levels for the remainder of the year. The risk to vertebrate scavengers and predators that rely on prey items that may consume spilled corn is also expected to be low. Estimate of risks to small mammals and birds (e.g., bobwhite quail and deer mouse) suggests that both groups would have to eat well above their daily food consumption rates to receive a lethal dose.

The risk to federally listed predators such as the ocelot, jaguarundi and aplomado falcon from the consumption of prey items containing ivermectin residues would also be considered low. The ocelot consumes primarily small mammals and birds while the jaguarundi consumes small mammals, birds, and reptiles (FWS, 2013; 2016). The aplomado falcon has a more varied diet consuming mammals, birds, reptiles, and insects with birds being the predominant food source (Hector, 1985; FWS, 2014). Most insect groups that the aplomado falcon would consume (e.g., moths, dragonflies, grasshoppers, wasps) would not be impacted by the use of ivermectin-treated corn because they do not use dung pellets from treated white-tailed deer, or other animals, to complete their life cycle (Hector, 1985; TPWD, 2013). The risk to scavengers and predators that may consume small mammals and birds that have consumed ivermectin-treated corn is expected to be low. Acute ivermectin toxicity data is not available for the ocelot or jaguarundi; however, these values can be approximated using the below equation (EPA, 2005):

$$\text{Adjusted } LD_{50} = LD_{50}\ (TW/AW)^{.25}$$

TW = body weight of the test animal (g)
AW = body weight of assessed animal (g)

The LD_{50} value used in these estimates was the lower value that was reported for the mouse (25 mg/kg). The body weight of the mouse was assumed to be 21 g. The average weight of the ocelot was 11.5 kg and for the jaguarundi, 6.4 kg (FWS, 2013; 2016). Using the above equation and the average body weights, the ocelot and jaguarundi adjusted LD_{50} values were 5.17 and 5.98 mg/kg, respectively. Consumption rate data for the ocelot states they consume between 0.56 and 0.84 kg of meat per day or an average of 0.7 kg/day. Assuming they only eat deer mice with an average weight of 21 grams an ocelot would consume approximately 33 mice per day or 6.27 mg ivermectin (33 mice * 0.19 mg ivermectin/mouse). The expected dose for the ocelot in mg/kg body weight would be 0.54 mg/kg. When comparing the expected dose to the estimated LD_{50}, the ocelot would have to consume approximately 9.6 times its daily consumption rate of mice to exceed the adjusted LD_{50} value. This exposure scenario assumes that ocelots only prey on mice that have consumed their maximum daily food rate with ivermectin-treated corn and that no depuration or metabolism of ivermectin occurred in the mice from the time they ingested the corn until they were consumed by the ocelot. Food consumption rates were not reported for the jaguarundi; however similar results would be expected based on the comparable adjusted LD_{50} values. Although there is some uncertainty in the estimated LD_{50}, values the conservative assumptions regarding exposure suggest that predatory mammals such as the ocelot and jaguarundi would be at low risk from the consumption of prey items that fed on ivermectin-treated corn. Risk to the aplomado falcon would also be low based on the conservative exposure assumptions and available avian toxicity data discussed above. In addition, the aplomado falcon has other food sources that would not be expected to contain ivermectin residues, further reducing the risk. Acute median lethality values do not account for potential sublethal risks to these species so there is some uncertainty regarding these types of impacts. However, the conservative estimate of exposure for scavengers and greater than 10 fold safety margins for direct acute risk suggest that sublethal risk to this group of non-target organisms would also be low. Chronic exposures are not anticipated because the feeders are checked weekly and any residual corn would be removed. In addition the feeders are used between February and July reducing exposure to any non-target mammals and birds that may serve as a food source for the ocelot, jaguarandi and aplomado falcon.

Indirect risk to insectivorous birds and mammals that feed on terrestrial invertebrates that may use deer droppings containing ivermectin is not anticipated. Most insectivorous birds, mammals, and reptiles are generalist feeders and would have other prey items available for consumption. In addition, the impact to dung-dependent invertebrates is variable and site specific, and may not result in any impacts to this group of invertebrates.

There is some risk to dung-dependent invertebrates, such as dung beetles and certain dipterans that would use droppings from deer that have consumed ivermectin-treated corn. These impacts would be localized to areas where feeders are placed and in cases where an invertebrate species relies solely on droppings from white-tailed deer. As stated above in the summary of ivermectin effects, the impacts to this group of invertebrates are variable based on several factors. The range of doses and effects that cause adverse effects are variable and depend on the type of formulation being tested, dosing method used, species dosed, and environmental variables in fields where the studies were conducted (Kruger and Scholtz, 1998a,b; Wall and Beynon, 2012). Any impacts would be primarily to dung beetles and flies that utilize deer droppings as part of their development and are sensitive to the effects of ivermectin. The spatial and temporal effects from the proposed use of ivermectin-treated corn are difficult to quantify because of the variability of effects, or lack of, in various studies exposing ivermectin to dung-dependent invertebrates. Available data would suggest there is risk to some invertebrates that would feed on deer droppings containing ivermectin; however, the range of sensitivities to various dung-dependent species suggests that not all species would be impacted (Rombke et al., 2010b; Steel and Wardhaugh, 2002; Floate et al., 2005; Blackhorn et al., 2013). This is supported by field level evaluations where ivermectin has been shown to have impacts to certain invertebrates resulting in impacts to diversity but with no changes in overall abundance (Wall and Beynon, 2012; Jochman et al., 2015). The potential for area-wide impacts to invertebrates that use deer droppings that contain ivermectin is also difficult to quantify; however, these types of impacts are expected to be low. Invertebrates sensitive to ivermectin would also utilize dung from other mammals that have not fed on ivermectin-treated corn. The greatest risk to dung-dependent beetles and flies will occur between February and July when the feeders are present. After that time the risk would decrease since white-tailed deer and other mammals are not feeding on ivermectin-treated corn and any droppings in the field containing ivermectin will degrade. The risks to sensitive invertebrates would be expected to last for approximately one to two weeks after the treated corn is removed based on a summary of studies that evaluated oral dosing of ivermectin and effects to certain dung dependent species (Floate et al, 2005). The risks to sensitive invertebrates would be localized to areas in proximity to the feeders. Deer may range over larger areas; however, they would be expected to congregate near feeders resulting in more deer droppings that could contain ivermectin in a smaller area. Deer that forage further away from the feeders after receiving a dose of ivermectin could also impact sensitive invertebrates but the risk would be lower because there would be dung from other animals that do not contain ivermectin.

The risk to aquatic organisms is expected to be negligible due to the lack of significant exposure. Treated corn is not expected to be transported to aquatic habitats in sufficient amounts that could result in risk to aquatic fauna. The feeder is a closed system that can only be accessed through spouts that contain baffles that can be adjusted to minimize spillage on the ground. A conservative estimate of spillage is 5% based on field observations. Assuming that a feeder is loaded with 300 pounds of whole kernel corn at a rate of 10 mg ivermectin per pound of corn, the total amount of ivermectin in the feeder would be 3,000 mg. Assuming 5% of the treated corn falls onto the ground during feeding, this would result in 150 mg of ivermectin available for transport to aquatic habitats from runoff. Conservative estimates from broadcast liquid pesticide applications suggest that up to 10% of the applied material may move off-site. The amount would be much lower in this example because the program is not using broadcast liquid treatments. However, 10% was used in this example as a very conservative estimate of off-site transport. The quantity of ivermectin (15.0 mg) entering an aquatic habitat one acre in size and one foot deep would result in a concentration of approximately 12 ng/L, assuming no degradation or dissipation. When compared to the available aquatic toxicity data for invertebrates, fish, and amphibians, the residue level is below the range of acute toxicity values for aquatic invertebrates, with the exception of the lowest reported Daphnia magna toxicity value, and is three orders of magnitude below the lowest effect concentration for aquatic vertebrates, suggesting a lack of risk to aquatic species (Figure 5-1). This value is also two orders of magnitude below the range of acute NOECs reported for fish (0.9-220 µg/L). The estimated residue is very conservative and would not occur in the field because it assumes there is no buffer between the site of the feeder and the aquatic habitat. In addition, it assumes that all of the ivermectin in the corn that enters the aquatic habitat would be present in the water and not degrade, which would not be the case because ivermectin preferentially binds to organic matter and degrades based on available environmental fate data (see Section 2.3). Degradation of ivermectin in water in the proposed area of treatment and in a shallow body of water would be expected to be rapid due to the rapid breakdown of ivermectin at higher temperatures and in the presence of light. The overly conservative assumptions were used in the estimate of an aquatic residue as a way to account for uncertainty in the available toxicity data while demonstrating safety to aquatic organisms.

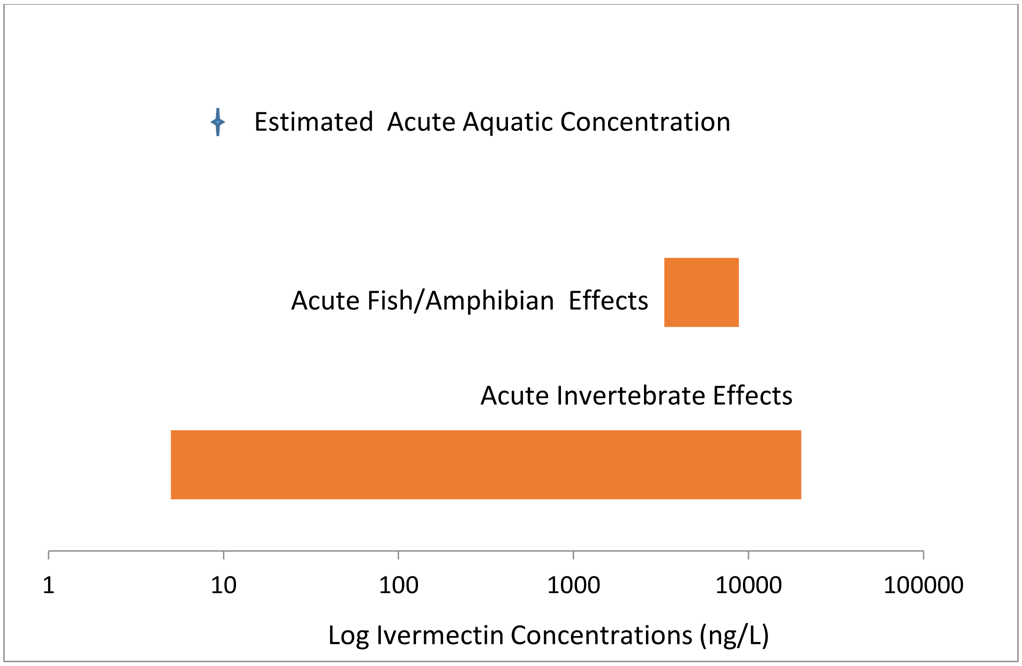

Figure 5-1. Acute aquatic risk characterization for ivermectin-treated corn.

The method of application and setting feeders a minimum of 50 feet from aquatic habitats suggests that any ivermectin-treated corn would be unlikely to enter surface water. In addition the environmental fate of ivermectin suggests that any material that would enter surface water would quickly dissipate and bind to organic matter or sediment, reducing bioavailability and risk to aquatic organisms. There is the potential for risk to aquatic organisms from droppings from deer that have consumed ivermectin-treated corn that enter surface water directly, or through runoff; however, the risk would be low because ivermectin would be bound to organic matter in the droppings. The risk to sediment-dwelling organisms would be greater than those invertebrates in the water column; however, the risk is also expected to be low for benthic invertebrates because the pathway for this exposure is not expected to be significant. Any impacts to sediment-dwelling invertebrates would be localized to those that would primarily consume deer droppings because other organic material would be available.

6.0 UNCERTAINTIES AND CUMULATIVE IMPACTS

The uncertainties associated with this risk evaluation arise primarily from lack of information about the effects of ivermectin, its formulations, metabolites, and potential mixtures to non-target organisms that can occur in the environment. These uncertainties are not unique to this assessment but are consistent with uncertainties in human health and ecological risk assessments with any environmental stressor. In addition, there is uncertainty in the number and location of feeding stations, which are based on number and density of deer in the program area.

Another area of uncertainty is the potential for cumulative impacts to human health and the environment from the proposed use of ivermectin in the CFTEP. Areas where cumulative impacts could occur are: 1) repeated worker and environmental exposures to ivermectin from program activities; 2) co-exposure to other chemicals with a similar mode of action; and 3) exposures to other chemicals in mixtures and how that may affect the toxicity of ivermectin.

Ivermectin is a widely used anti-parasitic drug in humans, livestock, and pets (Crump and Omura, 2011). There would be increased environmental loading from the use of ivermectin-treated corn for white-tailed deer where there are also ivermectin uses for cattle and other domestic animals. The impacts to white-tailed deer are expected to be incrementally negligible when put in context with other stressors because the dose of ivermectin is considered therapeutic and not intended to result in adverse effects. Domestic animals that are receiving ivermectin for other purposes are also not expected to have cumulative impacts resulting from the proposed use of ivermectin-treated corn because domestic animals will not be able to access the feeders. Cumulative impacts to aquatic organisms will also be negligible because there is an extremely low probability of exposure to aquatic habitats from the proposed use of ivermectin-treated corn.

Cumulative impacts to human health from the proposed use of ivermectin-treated corn are not anticipated because of the proposed use pattern. Human exposure and risk is very low for the general public. The probability of exposure is greatest for workers who mix and fill the feeders. However, the risk to this group of the population will be negligible based on the low risk of ivermectin when using the appropriate PPE. There is the potential for worker exposure to other chemicals that may be used in the CFTEP. Coumaphos is an organophosphate insecticide used to treat cattle for ticks that may vector cattle fever. Coumaphos affects the nervous system by inhibiting chlolinesterase (USEPA, 2006). Ivermectin and coumaphos have different modes of action and the literature does not indicate whether there could be synergism, potentiation, additive, or antagonistic effects from these two compounds. The potential for cumulative impacts related to exposure to both pesticides, in particular, to workers will be reduced by the use of PPE. Cumulative risk to the public from exposure to mixtures of both chemicals is also not anticipated because of the method of application, program controls, and restriction of public access to treatment areas. A study on pharmacokinetic interaction of ivermectin and spinosad in dogs indicates spinosad can increase the risk of ivermectin neurotoxicity by acting as a P-glycoprotein inhibitor (Dunn et al., 2011). Spinosad is a commonly used insecticide in agriculture and is used in other APHIS programs. The probability of exposure to the public and workers to both spinosad and ivermectin at the same time would be very low because of the use patterns and intended target for each pesticide. There has also been research to show synergistic effects between ivermectin and antibiotics (doxycycline, erythromycin, rifampicin, and azithromycin) in controlling body lice (Sangare et al., 2016). These interactions are not expected with the proposed use of ivermectin because treatments will be directed at wildlife that would not be receiving antibiotic treatment. These types of mixture exposures would not be anticipated for humans either because of the method of application and other measures to prevent exposure to the public and workers who mix ivermectin with corn and load the feeders.

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APPENDIX 2

Summary of and Responses to Comments Received on the Environmental Assessment Prepared for the Cattle Fever Tick Eradication Program Use of Ivermectin Corn

Issue: *Two commenters support the use of ivermectin-treated corn on all private properties and public lands that are at an increased risk of hosting cattle fever ticks.*

> Response: Program feeders are strategically placed where there have been cattle fever tick infestations in the vicinity of white-tailed deer populations. Feeders are stocked with ivermectin-treated corn annually from February through July so that deer have a large window of opportunity to feed on the corn. After consuming ivermectin-treated corn, it is beneficial for the deer to move around because they can pick up ticks that may be located elsewhere, and then those ticks will also die. Additionally, while it seems logical to treat all deer, rather than a few, the program does not have the resources to treat all deer in the affected counties. This treatment will be used, along with others, to create an integrated strategy for tick control.

Issue: *One commenter stated that he received a plan from APHIS that described how APHIS would supply non-medicated corn during the months when medicated corn was withdrawn from his ranch; however, non-medicated corn was never put in the feeders. The commenter believes supplying non-medicated corn would retain deer on ranches and minimize risk of reinfestation of treated deer with cattle fever ticks from neighboring ranches. Similarly, another commenter supported the use of non-medicated corn August through January to eliminate the need to move feeder locations based on deer population changes from herd movements.*

> Response: APHIS appreciates the comments from, and the landowners participating in, the CFTEP. Through established policies and procedures, we will attempt to treat all deer within a 2-mile range of where cattle fever ticks are discovered. There are occasions where this cannot be accomplished because of compliance challenges, variable deer population densities, resource limitations, and mission priorities at other locations. Concerning use of non-treated corn, when deemed strategic and as resources permit, APHIS does attempt to employ that tool as part of the management of potential cattle fever tick hosts.

Issue: *One commenter mentioned a rule stating that equine must receive deworming 30 days prior to slaughter. Based on this rule, the commenter wants to know how this would affect cattle and deer if they were slaughtered within 30 days of consuming ivermectin, and what impact would occur on animals and humans consuming these carcasses.*

Response: APHIS is uncertain of the commenter's reference to withdrawal period for deworming equine. There are no labeled ivermectin products for use in horses slated for food production. Horse slaughter for the production of food has not occurred in the United States since 2007, and APHIS is not familiar with the laws governing horse slaughter for human consumption in other countries. Regardless, APHIS does not anticipate that animals or humans will be negatively impacted by the use of ivermectin-treated corn in South Texas. APHIS has corresponded with the FDA, and the FDA does not object to the proposed extra-label use of ivermectin in deer. It should be noted that the FDA has approved ivermectin for human use to treat parasitic infections. As discussed in Appendix 1 of the EA, in a study where healthy adults received more than the intended dose of ivermectin, the results showed that ivermectin is generally well-tolerated by healthy adults with no indication of associated central nervous system toxicity at levels up to 10 times the highest FDA-approved dose (Guzzo et al., 2002).

To minimize the potential exposure of the general public to ivermectin, APHIS established a 60-day withdrawal period prior to the deer hunting season. A withdrawal period of 60 days was based on the extra-label use of ivermectin in food animals, and is 10 times longer than the elimination half-life of 6 days. Therefore, the potential exposure to ivermectin residues higher than the tolerance level from consumption of deer meat treated with ivermectin-corn for the general public is precluded by withdrawal of ivermectin-treated corn 60 days prior to the start of the hunting season. In addition, although cattle will not be fed ivermectin corn as part of this proposed action, for comparison purposes, various ivermectin products used in cattle have 35-48 day withdrawal periods (depending upon formulations).

Issue: *One commenter asked if nilgai would have access to the feeders.*

Response: While nilgai would have access to the feeders, APHIS noted in the EA that nilgai do not eat corn. Therefore, nilgai would not be treated with ivermectin in this manner. APHIS will, however, use periodic game cameras to monitor non-target species accessing the ivermectin corn feeders.

Issue: *One commenter is concerned that feeding ivermectin corn to deer will unintentionally kill beneficial insects that feed on deer feces. The commenter is also concerned that feeding ivermectin corn to deer could lead to resistant gastrointestinal nematodes that survive ivermectin treatment causing internal parasite issues that could lead to the death of individual animals.*

Response: As stated in the risk assessment in Appendix 1 of the EA, APHIS recognizes that there is some risk to dung-dependent invertebrates that would use droppings from deer that have consumed ivermectin-treated corn. The range of doses and effects that cause adverse effects are variable and depend on the formulation being tested, dosing method used, species dosed, and environmental variables; subsequently, not all species would be impacted. Any impacts would be primarily to dung beetles and flies that use deer feces as part of their development and are sensitive to the effects of ivermectin. These impacts would be localized to areas where feeders are placed.

Ivermectin is a widely used broad-spectrum, anti-parasitic drug in humans, livestock, and pets. Evidence of ivermectin-resistant gastrointestinal nematodes is increasing worldwide in goat and sheep flocks and bovine herds (Canul-Ku et al., 2012). Application of sub-therapeutic doses of ivermectin can reduce its efficacy and favors gastrointestinal nematode resistance (Canul-Ku et al., 2012). As discussed in Appendix 1, the feeding rate for deer is approximately 1% of body weight per day, or 1 pound per 100 pound deer per day. Based on this information, the daily intake dose of deer feeding on ivermectin-treated corn is approximately 0.22 mg/kg, which is an effective dose against ticks and gastrointestinal nematodes (Garris et al., 1991).

Frequency of ivermectin use can also contribute to gastrointestinal nematode resistance in farm animals. Selection pressure for resistance in gastrointestinal nematodes is increased if ivermectin is used for tick control every 30-35 days throughout the year (Canul-Ku et al., 2012). Use of ivermectin corn to treat deer is less likely to cause gastrointestinal nematode resistance because it will only be used a few months each year in limited areas. This use frequency will allow for maintenance of a nematode population that maintains the genes for susceptibility within its population, thereby reducing the development of gastrointestinal nematode resistance (Kenyon et al., 2009).

Issue: *One commenter urged APHIS to coordinate with private landowners when administering ivermectin-treated corn so that the agency does not infringe upon a landowner's ability to harvest wildlife. The commenter opposes extending the use of ivermectin-treated corn into months that would cause the withdrawal period of ivermectin-treated corn to overlap with the hunting season.*

Response: APHIS communicates with landowners prior to placing feeders on private property and is sensitive to a landowner's ability to harvest wildlife from their property. As such, APHIS will not extend the use of ivermectin-treated corn beyond the February through July window.

Issue: *One commenter suggested there should be a committee formed that consists of cattle ranchers, wildlife landowners, farmers, and veterinarians to identify solutions to the cattle fever tick problem. Another commenter mentioned the need to meet with landowners to address their concerns.*

Response: APHIS recognizes the need to communicate more broadly with individuals in South Texas regarding the CFTEP. A partner agency in the cattle fever tick response, the

Texas Animal Health Commission, has been spearheading communications, educational forums, and working group meetings with respective stakeholders.

Issue: *One commenter expressed concern about nilgai, suggesting that they should be protected on both private properties and refuges. Two commenters stated that nilgai provide a valuable resource to the community and removal of nilgai by helicopter can economically impact sporting good sales, hunting leases, meat processors, taxidermists, the sale of hunting licenses, and family memories. Another commenter further stated that he is strongly opposed to the removal of nilgai on state or federal lands adjacent to private lands.*

Response: This topic is outside of the scope of the "Cattle Fever Tick Eradication Program Use of Ivermectin Corn" Draft Environmental Assessment. This topic is, however, addressed more thoroughly in the "Population Reduction of Nilgai in the Boca Chica Beach, Bahia Grande, and Brownsville Navigation District Areas, Cameron County, Texas" Final Environmental Assessment published in September 2014.

Issue: *Two commenters suggested darting nilgai with ivermectin via helicopter as an alternative to lethally removing nilgai.*

Response: APHIS appreciates the suggestion to dart nilgai as an extension of the proposed program use of ivermectin corn to treat white-tailed deer. Cost, efficacy, and remote dart technologies would need to be studied prior to determining if this is a viable option and is outside the scope of this EA.

Issue: *One commenter asked how ivermectin will affect quail since quail are drawn to feeders with corn.*

Response: The risk assessment in Appendix 1 of the EA describes that by using body weight, daily food consumption rates, and ivermectin residues, a daily dose of ivermectin corn for bobwhite quail could be calculated. This data was then compared to the available toxicity data to determine whether consumption of ivermectin-treated corn would exceed effects levels. The assumption was that bobwhite quail would consume only ivermectin-treated corn and no other food material. Based on the calculation, bobwhite quail would have to consume approximately 1,342 times its daily food consumption rate to exceed the median lethality value. This information suggests that the acute risk to small non-target birds that consume ivermectin-treated corn would be low.

Issue: *One commenter stated that every USDA employee they had met stated that deer do not host cattle fever ticks. The commenter is supportive of treating them with ivermectin if their understanding is incorrect.*

Response: APHIS apologizes if any of its employees failed to properly communicate the role deer play in the life cycle of cattle fever ticks. Numerous studies have shown that deer are suitable hosts and reservoirs for cattle fever ticks (Graham et al., 1972, *in* Pound et al., 2010; George, 1990). In 1968, cattle fever ticks were discovered on white-tailed deer in ranches in Dimmit County, and southern cattle ticks were discovered on deer in other areas in later years, raising concern about the role of white-tailed deer and cattle fever tick outbreaks in the tick-free area (Giles, 2014). Since then, more evidence has accrued on the role of white-tailed deer as suitable cattle fever tick hosts and their importance in tick eradication efforts (Busch 2014). More information regarding the role of deer in distribution and maintenance of cattle fever ticks can be found in the "Cattle Fever Tick Eradication Program—Tick Control Barrier, Maverick, Starr, Webb, and Zapata Counties, Texas" Draft Environmental Impact Statement published in June 2013.

Issue: *One commenter asked APHIS to consider the following as part of their management program: 1) Identify the parameters used to determine length of the program; 2) Survey for resistance in parasites in deer; 3) Identify non-target species accessing ivermectin-treated corn directly or as part of the food chain; 4) Survey for development of resistance due to subtherapeutic dosing in susceptible parasites; 5) Publish the methods APHIS plans to use to determine the effectiveness of treatment; 6) Include Texas Parks and Wildlife Department during Endangered Species Act consultation activities; 7) Discuss alternatives to the use of ivermectin to deliver therapeutic doses to deer while reducing antiparasitic resistance pressures; and, 8) Provide surveillance activity findings (e.g., effectiveness, resistance development, non-target species impact) to the public periodically.*

Response: APHIS intends to implement the feeding of ivermectin-treated corn to white-tailed deer annually and has made this clarification in the Final EA. Briefly, the parameters used are locations where cattle fever ticks have been detected along the permanent quarantine line, or in adjacent areas of those counties that are determined to be at risk of incurring an infestation due to movements of tick-infested deer, or locations with identified infestations beyond the Permanent Tick Quarantine Zone. Another key parameter is a determination by veterinary epidemiologists that there is a risk of incurring infestations due to movements of tick-infested deer.

APHIS is aware of the potential for resistance to develop in gastrointestinal nematodes following the use of therapeutic (and potentially subtherapeutic) levels of an acaricide such as ivermectin. Since many nematodes are generalist parasites and have the potential to infect a broad range of hosts (Walker and Morgan, 2014), and ivermectin is frequently used to treat cattle in South Texas, conducting surveys for resistant parasites is unlikely to yield actionable data identifying the degree to which ivermectin-resistant gastrointestinal nematodes are occurring, if at all, as a result of APHIS' proposed action.

The primary measurement of effectiveness of this program will be cattle fever tick infestation rates or spread within, adjacent to, or beyond the Permanent Tick Quarantine Zone. The use of ivermectin-treated corn for deer is one component of APHIS' integrated pest management (IPM) programs and practices.

APHIS is legally required to consult with FWS during its ESA consultation activities, which it has done. FWS can involve additional parties in the consultation process if it chooses to do so. APHIS and TAHC periodically consult with the Texas Parks and Wildlife Department regarding native wildlife unrelated to federally-listed threatened and endangered species.

APHIS will use game cameras to occasionally monitor non-target species accessing the ivermectin-corn feeders. In addition, APHIS will continue to partner with stakeholders to assess science-based alternatives and potential improvements to controlling cattle fever ticks on deer while having minimal impact on the environment. APHIS will periodically provide surveillance activity findings to these stakeholder groups and the public.

Issue: *One commenter noted the confirmed presence of cattle fever ticks in Live Oak County on November 30, 2016, as well as the two infestations in Kleberg County in 2016. The commenter advocates for a process to be in place to efficiently add additional affected counties as the needs arise.*

Response: APHIS considered including all counties where cattle fever ticks could potentially be found in its documentation prepared for the ESA consultation and NEPA process but ultimately decided to move forward with the 10 counties discussed in the EA. After this decision, the confirmed presence of cattle fever ticks in Live Oak County occurred. Subsequently, APHIS worked with FWS to add Live Oak County, in addition to Kleburg and Kenedy counties, to the ESA consultation process. This will enable APHIS to move forward in a more expeditious manner if it chooses to place ivermectin-treated corn in these three additional counties.