

Received via email on October 7, 2016
From: Shalene McNeill, The Beef Checkoff

Comments:

Dear Dr. Boyd:

The Beef Checkoff appreciates the opportunity to submit scientific evidence to the Office of Health Assessment and Translation (OHAT) in response to the September 9, 2016, Federal Register (80 FR 62513-14) request for information regarding the possible evaluation of consumption of red meat, processed meat, and meat cooked at high temperatures for non-cancer health outcomes (e.g. development, reproductive, or immunological disorders).

OHAT “conducts evaluations to assess the evidence that environmental chemicals, physical substances, or mixtures (collectively referred to as “substances”) cause adverse health effects and provides opinions on whether these substances may be of concern given what is known about current human exposure levels. Assessments of potential adverse effects of environmental substances on reproduction or development”. (Source: <http://ntp.niehs.nih.gov/pubhealth/hat/index.html>)

The Beef Checkoff has submitted scientific evidence as public comment regarding cancer as a possible adverse health outcome associated with the consumption of red meat, processed meat, and meat cooked at high temperatures to the National Toxicology Program Report on Carcinogens and are also providing them to OHAT in separate submissions.

Additionally, the Beef Checkoff is not aware of any toxicological studies designed to investigate developmental, reproductive, or immunological disorders associated with meat consumption as part of a complete diet.

Below is a list of recent (last 5 years) literature identifying the benefits of meat for child development and maternal health.

*Complementary Feeding

Krebs NF, et al. Comparison of complementary feeding strategies to meet zinc requirements of older breastfed infants. Am J Clin Nutr. 2012 Jul;96(1):30-5.

In this study, 45 exclusively breastfed 5-month-old infants were randomized to 1 of 3 feeding groups: commercially available pureed meat (beef and gravy), iron- and zinc-fortified infant cereal (IZFC), or iron-only fortified infant cereal (IFC) as the first and primary complementary food through 9-10 months of age. Mean daily zinc intakes were significantly greater for the meat and IZFC groups than for the IFC group and only intakes in meat and IZFC groups met estimated average requirements. Mean total absorbed zinc amounts was greater in the meat and IZFC groups than the IFC group. The researchers conclude that zinc requirements for older breastfed-only infants are unlikely to be met without the regular consumption of either meats or zinc-fortified foods.

Krebs NF, et al. Randomized controlled trial of meat compared with multimicronutrient-fortified cereal in infants and toddlers with high stunting rates in diverse settings. *Am J Clin Nutr.* 2012 Oct;96(4):840-7.

In cluster randomized efficacy trial conducted in the Democratic Republic of Congo, Zambia, Guatemala, and Pakistan, infants 6 to 18 mo of age received daily portions of study foods (30-45g lyophilized beef or an equicaloric multimicronutrient-fortified cereal). A total of 532 and 530 participants from the meat and cereal arms, respectively, completed the study. Unfortunately, poor linear growth already evident at 6 mo was too poor that either intervention was unable to reverse this trend, suggesting for multifaceted interventions beginning in the pre- and early postnatal periods to prevent further linear growth failure in older infants and toddlers living in impoverished environments.

Krebs NF, et al. Effects of different complementary feeding regimens on iron status and enteric microbiota in breastfed infants. *J Pediatr.* 2013 Aug;163(2):416-23.

In this study, 45 exclusively breastfed 5-month-old infants were randomized to 1 of 3 feeding groups: commercially available pureed meat (beef and gravy), iron- and zinc-fortified infant cereal, or iron-only fortified infant cereal as the first and primary complementary food through 9-10 months of age. More than one-quarter (27%) of the infants had a low serum ferritin level, and 36% were mildly anemic. Infants in the cereal groups had 2-3 fold greater daily iron intakes compared to the meat group, but all infants had similar iron status. Complementary feeding, including iron exposure, influenced the development of the enteric microbiota.

Olaya GA, et al. Efficacy and safety of new complementary feeding guidelines with an emphasis on red meat consumption: a randomized trial in Bogota, Colombia. *Am J Clin Nutr.* 2013 Oct;98(4):983-93. The researchers tested new complementary feeding guidelines emphasizing meat as a source of iron and zinc for infants living in poor socioeconomic circumstances in Bogota, Colombia. Seventy six infants who were exclusively breastfed for ≥ 4 mo were randomly assigned at 6 mo of age to a control group [CG; current advice] or intervention group (new guidelines group [NGG; with counseling to 1) continue breastfeeding, 2) offer red meat ≥ 3 d/wk, and 3) offer fruit and vegetables daily]). The new guidelines showed efficacy with higher red meat intake and positive effects on hemoglobin and hematocrit than the current guidelines.

Tang M, Krebs NF. High protein intake from meat as complementary food increases growth but not adiposity in breastfed infants: a randomized trial. *Am J Clin Nutr.* 2014 Nov;100(5):1322-8.

In this study, 45 exclusively breastfed 5-month-old infants were randomized to 1 of 3 feeding groups: commercially available pureed meat (beef and gravy), iron- and zinc-fortified infant cereal (IZFC), or iron-only fortified infant cereal (IFC) as the first and primary complementary food through 9-10 months of age. In a secondary analysis, anthropometric measures and diet records of 14 from the Meat group and 28 from the Cereal group were assessed at 9 mo of age. In breastfed infants, higher protein intake from meats was associated with greater linear growth and weight gain but without excessive gain in adiposity, suggesting that potential risks of high protein intake may differ between breastfed and formula-fed infants and by the source of protein.

Tang M, et al. Meat as complementary food for older breastfed infants and toddlers: a randomized, controlled trial in rural China. *Food Nutr Bull.* 2014 Dec;35(4 Suppl):S188-92.

In this cluster-randomized, controlled study, the researchers compared the difference in anthropometric measurements of rural Chinese infants and toddlers 6 to 18 months of age who received a daily supplement of meat or cereal for 12 months. The subjects were provided a daily supplement of either meat (boiled ground pork) (n = 514, 20 clusters) or rice cereal (n = 957, 40 clusters) as a first complementary food at 6 months of age. After 12 months of intervention, linear growth was modestly greater in

the meat group than in the cereal group and a smaller decrease in length-for-age z-score (LAZ) over time, after adjustment for baseline length, LAZ, maternal education, work status, and maternal height and weight. LAZ was substantially negative at 6 months, and the intervention did not prevent ongoing decline over the course of the study.

Ongoing research:

Research Study Title: The long-term effects of meat as an early complementary food in infancy on body composition and gut microbiome in young children: a follow-up study. The researchers (Krebs and co-workers) indicate that the primary objective of this ongoing study is to evaluate the long-term effect of a high protein intake from meat during infancy by following the participants in a previous randomized control trial and assessing their growth, body composition, and gut microbiome. Krebs and co-workers hypothesize that the greater increases of LAZ and WAZ observed in the meat group when they were infants will be associated with greater HAZ and WAZ, without increased BMI or adiposity, in the meat group participants when they are in their early childhood. In addition, Krebs and co-workers also hypothesize that the gut microbiome profile will also be different between participants who were originally in meat or cereal groups.

Research Study Title: Protein consumption from meat vs. dairy as complementary foods on infant growth, body composition and gut microbiome: a controlled feeding study. The investigators (Krebs and co-workers) indicate that the primary objective of this ongoing study is to compare linear growth, body composition and gut microbiota composition in formula fed infants consuming a high-protein, complementary diet with protein mainly from meat or dairy. Krebs and co-workers hypothesize that the research study infants consuming dietary protein from meat over the 1st year of life will have a greater linear growth compared with research study infants consuming dairy. Krebs and co-workers hypothesize that consumption of dairy will result in accelerated weight and adiposity gain over time among research study infants compared to meat and microbiota profile will contain more energy harvesting, less health-promoting bacteria in the high protein dairy group compared with meat group.

Research Study Title: Protein quality early in life: potential mechanisms of impact on growth and later obesity development The investigators (Krebs and co-workers) indicate that the primary

objectives of this ongoing study are to evaluate whether the differences in growth between groups of infants from 6 to 12 months of age persists and to provide mechanistic insights of the observed greater linear growth in the infants fed meat and increased risk of being overweight in infants fed dairy. Krebs and co-workers hypothesize that the infants in the meat group will continue to have greater linear growth at 18 and 24 months, compared with infants in the dairy group. Krebs and co-workers also hypothesize that infants in the dairy group will continue to demonstrate greater WLZ and BMI Z scores (risk factors for later-in-life obesity), and impaired linear growth at 18 and 24 months of age.

*Children/Adolescents

Neil CE, et al. Nutrient contribution of total and lean beef in diets of US children and adolescents: National Health and Nutrition Examination Survey 1999-2004. *Meat Sci.* 2011 Mar;87(3):250-6.

Using data from NHANES 1999-2004, the nutritional contribution of total beef and lean beef to the diet of US children and adolescents was evaluated. Dietary recall data was collected from children 4-8 years of age [y] (n=2474), 9-13 y (n=3273), and adolescents 14-18 y (n=4044). Lean beef was defined as beef with ≤ 9.28 grams [g] fat/100 g (excess was discretionary fat). The consumption of lean beef contributed significantly to intake of protein and many key nutrients such as vitamins B6 and B12, zinc, iron, niacin, phosphorus, and potassium by US children and adolescents without providing significantly to intakes of total fat, saturated fatty acids, or sodium.

Long JK, et al. Meat and milk intakes and toddler growth: a comparison feeding intervention of animal-source foods in rural Kenya. *Public Health Nutr.* 2012 Jun;15(6):1100-7.

In this 5-month comparison feeding intervention study the effects of animal-source foods on toddler growth were assessed. One of three millet-based porridges randomized to 18 feeding stations served 274 children aged 11-40 months in Embu, Kenya. Feeding stations served plain millet porridge (Plain group), porridge with milk (Milk group) or porridge with beef (Meat group). The milk and meat porridges did not have a significantly greater effect on growth than plain porridge in this undernourished population. Linear growth was influenced by more than energy intakes, as the Plain group's total body weight-adjusted

energy intakes were significantly greater than the Meat group's, although linear growth did not differ. Energy intakes may be more important for growth in arm muscle. The diverse age distribution in the study makes interpretation difficult.

Neumann CG, et al. Meat supplementation increases arm muscle area in Kenyan schoolchildren. *Br J Nutr.* 2013 Apr 14;109(7):1230-40.

This cluster-randomised feeding trial evaluated the impact of mid-morning snacks containing animal source foods (ASF) on arm muscle area growth over two school years (1999 to 2001). Twelve primary schools in rural Kenya were randomly assigned to one of three isoenergetic feeding groups (Meat group = a local plant-based stew (githeri) with meat (85 g of ground beef containing 10-12% fat), Milk group = githeri plus whole milk or Plain group = githeri with added oil) or a Control group receiving no intervention feeding. The meat group showed the steepest rates of gain in mid-upper-arm circumference (MUAC) and mid-upper-arm muscle area (MAMA) over time, and the milk group showed the next largest significant MUAC and MAMA gain compared with the plain githeri and control groups. The meat group showed the least increase in triceps skinfold (TSF) and mid-upper-arm fat area (MAFA) of all groups. The results of the present study have implications for ameliorating wasting among HIV/AIDS patients who have severe loss of lean body mass and multiple nutrition deficiencies. Animal-source foods of a wide variety, from insects to small mammals, can be a sustainable strategy for improvement of dietary quality, especially in poor areas of developing countries.

Hulett JL, et al. Animal source foods have a positive impact on the primary school test scores of Kenyan schoolchildren in a cluster-randomised, controlled feeding intervention trial. *Br J Nutr.* 2014 Mar 14;111(5):875-86.

This cluster-randomised feeding trial evaluated the impact of mid-morning snacks containing animal source foods (ASF) on standardised test scores and nutrient intake over two school years (1999 to 2001). Twelve primary schools in rural Kenya were randomly assigned to one of three isoenergetic feeding groups (Meat group = a local plant-based stew (githeri) with meat (85 g of ground beef containing 10-12% fat), Milk group = githeri plus whole milk or Plain group = githeri with added oil) or a Control group receiving no intervention feeding. Children receiving ASF (meat and milk) had greater improvements in test scores. Children

in the Meat group showed significant improvements in test scores than the other groups, and the Milk group showed significantly greater improvements in test scores than the Plain and Control groups. Folate, iron, energy per body weight, vitamin B₁₂, Zn and riboflavin intake were significant contributors to the change in test scores.

Bradlee ML, et al. Lean red meat consumption and lipid profiles in adolescent girls. *J Hum Nutr Diet*. 2014 Apr;27 Suppl 2:292-300.

Using data from the National Heart Lung and Blood Institute Growth and Health Study, diets of 1461 girls who were followed for 10 years, starting at 9-10 years of age was assessed. These analyses suggest that lean red meat may be included in a healthy adolescent diet without unfavourable effects on lipid values. After adjusting for age, race, socioeconomic status, height, activity level, hours of television per day, and intakes of whole grains and dairy foods using multivariable modelling, girls consuming over 6 oz lean red meat per week combined with two or more servings of fruit/nonstarchy vegetables per day had lower LDL-Cholesterol levels than girls with lower intakes of lean red meat and fruit/nonstarchy vegetables. In addition, girls with higher intakes of both were 33% less likely to have elevated LDL-Cholesterol levels and 41% less likely to have an elevated LDL:HDL ratio at the end of adolescence.

Jancey JM, et al. Dietary outcomes of a community based intervention for mothers of young children: a randomised controlled trial. *Int J Behav Nutr Phys Act*. 2014 Sep 23;11:120. This randomised controlled trial aimed to increase the level of fruit, vegetable and fibre intake and decrease the fat and sugar consumption of mothers with young children (0-5 years) via the playgroup setting in Perth, Western Australia. Those in the intervention group received a 6-month multi-strategy primarily home-based physical activity and nutrition program. The intervention group showed moderate positive improvements in the overall consumption of fat, fibre, fruit and vegetables, wholegrain, dairy products and lean meat and chicken, when compared to the control group.

Ernst J, et al. High-nutrition biscuits to increase animal protein in diets of HIV-infected Kenyan women and their children: a study in progress. *Food Nutr Bull*. 2014 Dec;35(4 Suppl):S198-204.

In a randomized trial the effect of meat in the diet of drug-naïve, HIV-infected rural Kenyan women on changes in weight, lean body mass, morbidity, nutritional status, and activities of daily living of the women and growth and development of their children were evaluated. The Kenyan women and their children were provided one of three supplemental isocaloric biscuits: one with added dried beef another with added soybean flour, and a wheat biscuit to serve as a control biscuit. Data analysis for clinical outcomes of the trial is ongoing but preliminary data shows the meat biscuits provided more lysine, vitamin B12, and bioavailable zinc and the soybean biscuits provided more total and absorbable iron; however, higher fiber and phytate contents may inhibit nutrient absorption. The biscuits were well received by the adults and children, and can be produced locally with available, simple, affordable technology.

*Maternal Health

Moran LJ, et al. A decrease in diet quality occurs during pregnancy in overweight and obese women which is maintained post-partum. *Int J Obes (Lond)*. 2013 May;37(5):704-11.

This prospective cohort study performed a comprehensive assessment of diet quality in 301 overweight and obese women during pregnancy and early post-partum. The women completed a food frequency questionnaire at study entry (10-20 weeks gestation), 28 weeks gestation, 36 weeks gestation and 4 months post-partum for assessment of macronutrient and micronutrient intake and diet quality by the Healthy Eating Index (HEI). The HEI was of below average quality in 31.0% of women at baseline. Dietary quality decreased across pregnancy and was maintained at a reduced level in the early post-partum period in overweight and obese women. The HEI decrease occurred in association with decreases in the milk, meat and unsaturated oil components, and increases in the proportion of energy from solid fats, alcohol and added sugars. Dietary interventions aimed at improving diet quality should be targeted to early pregnancy and post-partum.

Yan J, et al. Pregnancy alters choline dynamics: results of a randomized trial using stable isotope methodology in pregnant and nonpregnant women. *Am J Clin Nutr*. 2013 Dec;98(6):1459-67.

This study used stable isotope methodology to examine the effects of pregnancy on choline partitioning and the metabolic activity of choline-related pathways. Healthy third-trimester pregnant (n = 26; initially week 27 of gestation) and nonpregnant (n = 21)

women consumed 22% of their total choline intake (480 or 930 mg/d) as methyl-d₉-choline (supplemental choline chloride) for the final 6 wk of a 12-wk feeding study. The enhanced use of choline for phosphatidylcholine shows the substantial demand for choline during late pregnancy. Given that beef is a significant source of choline, beef consumption among pregnant woman may improve maternal/fetal pregnancy outcomes.