Testimony on HPAI and Raw Milk 7 April 2024

I, Margaret E. (Peg) Coleman, MS, am a medical microbiologist and risk analyst specializing in benefit and risk assessments for microbial pathogens and food safety. My credentials include two graduate degrees in medical microbiology and biochemistry and more than 30 years of experience in microbial risk analysis, initially for USDA and currently as a consultant. My appended resume documents previous expert testimony for multiple court cases and an extensive body of work relevant to raw milk microbes beginning in 2014. My expertise in microbial risk analysis is recognized in the US and internationally, evidenced by my recognition as a Fellow of the Society for Risk Analysis (SRA) in 2020, as an elected Counselor of SRA (2022-2024), and as a member of the Advisory Board of the Raw Milk Institute (RAWMI).

Recent risk communications from CDC (https://stacks.cdc.gov/view/cdc/152747), FDA (https://www.fda.gov/food/milk-guidance-documents-regulatory-information/questions-and-answers-regarding-milk-safety-during-highly-pathogenic-avian-influenza-hpai-outbreaks), and USDA (file:///C:/Users/colem/Documents/CASES/Milk/antiViralPapers/USDA%20FDA%20CDC%20Share%20UpdateHPAIdetecDairyCattle%20_%20APHIS.html) regarding transmission of highly pathogenic avian influenza virus or HPAI (subtype H5N1) to humans via raw milk include no supporting evidence of viral transmission from raw milk to humans in the peer-reviewed literature. An extensive body of scientific evidence from the peer-reviewed literature introduced herein does not support the assumption by these US government agencies that HPAI transmits to humans via milkborne or foodborne routes and causes disease. Nor does the scientific evidence support the recommendation that consumers should avoid raw milk and raw milk products.

Although HPAI was detected in milk from ill cows, no evidence supports milkborne transmission of HPAI to humans. In fact, CDC and USDA reported that the HPAI strains recently isolated in the US lack the genetic markers for viruses adapted to infect humans. Further, the fact sheet prepared by the World Health Organization (WHO, https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic) lists the following key facts i) "animal influenza viruses are distinct from human influenza viruses and do not easily transmit to and among humans;" and sustained person-to-person transmission is not demonstrated. In summary, of all the transmission sources reported in surveillance systems by CDC and other government agencies (animal contact, environmental, foodborne, person-to-person, and waterborne), the only demonstrated transmission source for HPAI is animal contact.

Where is the direct supporting scientific evidence on mechanisms relevant to HPAI transmission via milk to humans? The peer-reviewed literature includes many relevant studies, including appended references.

First, consider peer-reviewed studies demonstrating antiviral properties of a suite of bioactive components of raw mammalian milks, including bovine milk (Panon et al., 1987; Tache et al., 1995; Taha et al., 2010; Schlusselhuber et al., 2018; Oda et al., 2021; Wang et al., 2021; Kaplan et al., 2022; Gallo et al., 2022, 2024; Singh et al., 2023; Santos et al., 2024). Multiple researchers note that some of the antiviral components of milk listed in the text box on the right likely function synergistically, meaning effects are greater in combination than independently, an observation particularly relevant in

<u>Some Milk Components with Antiviral Activity</u>

- Angiogenin
- Casein
- Lactadherin
- Lactoferricin
- Lactoferrin
- Lactoferampin
- α-, β-lactoglobulin
- Lactoperoxidase
- Lysozyme
- Milk mucin
- Milkisin
- Oligosaccharides
- Secretory IgA, IgG, IgM
- Serum albumin
- Tenacin-C

complex gut ecosystems of humans that include innate and adaptive immune systems. Many of these bioactive components of raw milk are also sensitive to heat and may be absent, inactive, or present in lower concentrations in pasteurized milks. Considering the extensive literature on antiviral activity in milk, clinical researchers (Francese et al., 2023) applied deep scientific knowledge to recommend that infants not be deprived of raw breastmilk due to the presence of viruses. The benefits of feeding raw breastmilk including its antiviral components to infants outweighs the very small risk of infection, from their perspective as clinical researchers, one associated with the Italian Association of Human Milk Banks.

Next, consider the gauntlet of defenses against foodborne pathogens in the human digestive tract (Buchanan et al., 2009; Lockhart et al., 2022; Wan et al., 2023). These defenses include physical (stomach acidity, peristalsis), chemical (digestive enzymes), and cellular (innate and adaptive immune system, microbiota) factors that, acting simultaneously or sequentially, inactivate pathogens, including viruses, and/or suppress infectivity and virulence of ingested pathogens. Sangsiriwut and colleagues (2018) note that HPAI is an enveloped virus, susceptible to disruption and degradation in stomach acids, unlike the 16 viruses known to be transmitted to human by the oral route (Lockhart et al., 2022).

Host chemical and cellular defenses include: complement; defensins; enzymes; interferons; interleukins; pattern recognition receptors (Toll-like receptors 3, 4, and 7; NOD-like receptors; RIG-1 receptors); and an array of host cells (dendritic cells, B cells, intestinal epithelial cells, macrophages, monocytes, natural killer cells, T cells) and cells of the gut-associated microbes or microbiota. Also, the gut microbiota include not only commensal (non-pathogenic) bacteria, but also commensal viruses that can modulate infectivity and virulence of pathogens (Pavia et al., 2023).

Now, consider that the microbial ecology of raw milks including antiviral activity as described briefly above aligns with recent CDC data for all transmission sources from 2005 to 2020 (Stephenson et al., 2024). This CDC dataset included 3,807 milkborne illnesses (2,111 associated with pasteurized milk) linked to bacterial pathogens, but lacks any viral illness associated with milk, raw or pasteurized. The predominant virus in this CDC dataset was norovirus, associated with 8,199 illnesses from leafy greens reported over this 16-year period. No norovirus illnesses or any other viral illnesses were reported in milk.

What is known about HPAI transmission to humans is that it is rare, requiring prolonged direct contact with infected, sick, and dead animals, generally birds, that can lead to mild flu-like symptoms or eye inflammation, some progressing to fatal infections (WHO, 2024). Again, HPAI in humans is linked to transmission via animal contact.

It seems that one TX farm worker handling ill chickens and dairy cows became infected and developed one symptom, eye redness (conjunctivitis), consistent with transmission by animal contact in 2024.

HPAI has been detected in dairy cows in Texas, Kansas, New Mexico and Michigan as of April 2. The affected dairy animals have recovered with little to no associated mortality reported.

Cross-disciplinary evidence demonstrates that raw milk from healthy cows is not inherently dangerous, consistent with the CDC evidence of trends for 2005-2020 (Stephenson et al., 2024) and evidence of benefits and risks (Dietert et al., 2022). There is no scientific evidence that HPAI in raw milk causes human disease.

Please permit consumers to choose real milk, fresh and unprocessed, complete with its natural beneficial microbiota.

References

1. Buchanan RL, Havelaar AH, Smith MA, Whiting RC, Julien* E. The key events dose-response framework: its potential for application to foodborne pathogenic microorganisms. Critical Reviews in Food Science and Nutrition. 2009 Sep 22;49(8):718-28.

2. Dietert RR, Coleman ME, North DW, Stephenson MM. Nourishing the human holobiont to reduce the risk of non-communicable diseases: a cow's milk evidence map example. Applied Microbiology. 2021 Dec 30;2(1):25-52.

3. Francese R, Peila C, Donalisio M, Lamberti C, Cirrincione S, Colombi N, Tonetto P, Cavallarin L, Bertino E, Moro GE, Coscia A. Viruses and human milk: transmission or protection?. Advances in Nutrition. 2023 Aug 20.

4. Gallo V, Giansanti F, Arienzo A, Antonini G. Antiviral properties of whey proteins and their activity against SARS-CoV-2 infection. Journal of Functional Foods. 2022 Feb 1;89:104932.

5. Gallo V, Arienzo A, Tomassetti F, Antonini G. Milk bioactive compounds and gut microbiota modulation: the role of whey proteins and milk oligosaccharides. Foods. 2024 Mar 16;13(6):907.

6. Lockhart A, Mucida D, Parsa R. Immunity to enteric viruses. Immunity. 2022 May 10;55(5):800-18.

7. Kaplan M, Şahutoğlu AS, Sarıtaş S, Duman H, Arslan A, Pekdemir B, Karav S. Role of milk glycome in prevention, treatment, and recovery of COVID-19. Frontiers in Nutrition. 2022 Nov 8;9:1033779.

8. Oda H, Kolawole AO, Mirabelli C, Wakabayashi H, Tanaka M, Yamauchi K, Abe F, Wobus CE. Antiviral effects of bovine lactoferrin on human norovirus. Biochemistry and Cell Biology. 2021;99(1):166-72.

9. Panon G, Tache S, Labie C. Antiviral substances in raw bovine milk active against bovine rotavirus and coronavirus. Journal of Food Protection. 1987 Oct 1;50(10):862-7.

10. Pavia G, Marascio N, Matera G, Quirino A. Does the human gut virome contribute to host health or disease?. Viruses. 2023 Nov 17;15(11):2271.

11. Sangsiriwut K, Uiprasertkul M, Payungporn S, Auewarakul P, Ungchusak K, Chantratita W, Puthavathana P. Complete Genomic Sequences of Highly Pathogenic H5N1 Avian Influenza Viruses Obtained Directly from Human Autopsy Specimens. Microbiol Resour Announc. 2018. 7(22):e01498-18. doi: 10.1128/MRA.01498-18. PMID: 30533850; PMCID: PMC6284082.

12. Santos I, Silva M, Grácio M, Pedroso L, Lima A. Milk antiviral proteins and derived peptides against zoonoses. International Journal of Molecular Sciences. 2024. 25(3):1842.

13. Schlusselhuber M, Godard J, Sebban M, Bernay B, Garon D, Seguin V, Oulyadi H, Desmasures N. Characterization of milkisin, a novel lipopeptide with antimicrobial properties produced by Pseudomonas sp. UCMA 17988 isolated from bovine raw milk. Frontiers in Microbiology. 2018. 9:355822.

14. Singh P, Hernandez-Rauda R, Peña-Rodas O. Preventative and therapeutic potential of animal milk components against COVID-19: A comprehensive review. Food Science & Nutrition. 2023. 11(6):2547-79.

15. Stephenson MM, Coleman ME, Azzolina NA. Trends in burdens of disease by transmission source (usa, 2005–2020) and hazard identification for foods: focus on milkborne disease. Journal of Epidemiology and Global Health. 2024 Mar 28:1-30.

16. Tache S, Benkaddour M, Corpet DE. Rotavirus inhibitor and recovery in raw bovine milk. Journal of Food Protection. 1995 Apr 1;58(4):434-8.

17. Taha SH, Mehrez MA, Sitohy MZ, Abou Dawood AG, Abd-El Hamid MM, Kilany WH. Effectiveness of esterified whey proteins fractions against Egyptian Lethal Avian Influenza A (H5N1). Virology Journal. 2010 Dec;7:1-4.

18. Wan T, Wang Y, He K, Zhu S. Microbial sensing in the intestine. Protein & Cell. 2023 Nov 1;14(11):824-60.

19. Wang X, Yue L, Dang L, Yang J, Chen Z, Wang X, Shu J, Li Z. Role of sialylated glycans on bovine lactoferrin against influenza virus. Glycoconjugate Journal. 2021 Dec 1:1-8.