ONGOING WORK TO ENSURE CONTINUED EFFECTIVENESS OF FEDERAL-STATE MILK SAFETY SYSTEM

The U.S. Department of Agriculture (USDA), the U.S. Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC), along with state partners, continue to investigate an outbreak of highly pathogenic avian influenza (HPAI) virus impacting dairy cows in multiple states. Infection with the virus is causing decreased lactation, low appetite, and other symptoms in affected cattle.

The FDA and USDA have indicated that based on the information currently available, our commercial milk supply is safe because of these two reasons: 1) the pasteurization process and 2) the diversion or destruction of milk from sick cows.

The pasteurization process has served public health well for more than 100 years. Pasteurization is a process that kills harmful bacteria and viruses by heating milk to a specific temperature for a set period of time to make milk safer. Even if virus is detected in raw milk, pasteurization is generally expected to eliminate pathogens to a level that does not pose a risk to consumer health. However, pasteurization is different than complete sterilization; sterilization extends shelf life but is not required to ensure milk safety. While milk is pasteurized, not sterilized, this process has helped ensure the health of the American public for more than 100 years by inactivating infectious agents.

Nearly all (99%) of the commercial milk supply that produced on dairy farms in the U.S. comes from farms that participate in the Grade "A" milk program and follow the Pasteurized Milk Ordinance (PMO), which includes controls that help ensure the safety of dairy products. Pasteurization and diversion or destruction of milk from sick cows are two important measures that are part of the federal-state milk safety system.

There are a number of collective activities being undertaken to ensure the continued effectiveness of the federal-state milk safety system. In addition to these specific research activities, the FDA is collaborating closely with CDC's food safety group, as well as its surveillance team that's monitoring emergency department data and flu testing data for any unusual trends in flu-like illness, flu, or conjunctivitis. To date, surveillance systems do not show any unusual trends or activity.

As noted by USDA and some press reports from the World Health Organization (WHO) and other sources, the presence of the virus has been detected in raw milk. Based on available information, pasteurization is likely to inactivate the virus, however the process is not expected to remove the presence of viral particles. Therefore, some of the samples collected have indicated the presence of HPAI using quantitative polymerase chain reaction (qPCR) testing.

During the course of the outbreak, the FDA has been evaluating milk from affected animals, in the processing system, and on the shelves. We are completing a large representative national sample, to better understand the extent of these findings. Because qPCR findings do not represent actual virus that may be a risk to consumers, the FDA is further assessing any positive findings through egg inoculation tests, a gold-standard for determining viable virus. To date, we have seen nothing that would change our assessment that the commercial milk supply is safe. Results from multiple studies will be made available in the next few days to weeks.

Sound science is critical to informing public health decisions like those made by the FDA related to food safety and we take this current situation and the safety of the milk supply very seriously. We recognize the importance of releasing further, actionable information.

Review of Available Data

Given that the detection of H5N1 in dairy cows is a novel and evolving situation, no studies on the effects of pasteurization on HPAI viruses (such as H5N1) in bovine milk have previously been completed although considerable scientific literature is available that has informed our current understanding.

The established pasteurization process set forth in the PMO provides specific times and temperature requirements[i] for effective pasteurization of known pathogens in the milk supply. Data from previous studies[ii,iii] that serve as the underpinnings of the FDA's current milk supply safety assessment show that pasteurization is very likely to effectively inactivate heat-sensitive viruses, like H5N1, in milk from cows and other species. Additionally, data[iv,v,vi] shows thermal inactivation of HPAI (H5N1) has been successful during the pasteurization process for eggs, which occurs at lower temperatures than what is used for milk.

Ongoing Research

U.S. government partners have been working with deliberate speed on a wide range of studies looking at milk along all stages of production -- on the farm, during processing and on shelves -- using well-established methodologies used previously to confirm pasteurization effectiveness for known pathogens.

This work is a top priority, and we are proceeding in an efficient, methodical, and scientific fashion to ensure the continued effectiveness and safety of the federal-state milk safety system.

Laboratory benchtop tests are the first part of this ongoing work. This includes testing laboratory generated samples inoculated with high levels of a recently isolated and closely related avian flu virus and samples of raw, unpasteurized milk directly from cows in affected herds with and without symptoms to understand how, and at what levels, heat treatment (pasteurization) inactivates the virus.

While this information is important, this testing alone cannot provide a complete picture as these samples are not representative of what we would expect to see in the real-world from milk routed to pasteurization and processing for commercial use.

In addition to lab testing, a critical step in the scientific confirmation process includes testing of milk that is representative of real-world scenarios in which milk is typically pooled in large amounts from numerous healthy cows from numerous farms before pasteurizing and processing.

Work is underway to test samples of milk in systems that represent current industry practices using the range of temperature and time combinations that are used in pasteurization processes.

Additional analysis is underway of milk on store shelves across the country in addition to work to evaluate any potential differentiation for various types of dairy products (e.g., whole milk, cream).

We are aware that universities or other entities are conducting work in this area, particularly universities and consortia supported by the National Institutes of Health. We look forward to reviewing all results generated from various scientific studies, testing methods and the product(s) used as we continue assessing all the data and information available. We are committed to collaborating with the broad community to come to sound scientific conclusions regarding this situation -- which it's important to understand takes time.

Data Considerations

Multiple tests are used to assess the safety of food items. Understanding how and why different methodologies are used and work, as well as how results fit into the larger picture, is critical to interpret any findings.

- **Quantitative polymerase chain reaction (qPCR)** is a screening tool used to determine the presence or absence of an organism's genetic material in a sample. A positive qPCR means that the genetic material from the targeted pathogen was detected in the sample, but that **does not** mean that the sample contains an intact, infectious pathogen. That's because qPCR tests will also detect the residual genetic material from pathogens killed by heat, like pasteurization, or other food safety treatments. **Importantly, additional testing is required to determine whether intact pathogen is still present and if it remains infectious, which determines whether there is any risk of illness associated with consuming the product.**

- **Embryonated Egg Viability Studies** are considered the "gold standard" for sensitive detection of active, infectious virus. These studies are one of the types of additional tests necessary following PCR testing. These studies are done by injecting an embryonated chicken egg with a sample and then evaluating to see whether any active virus replicates. While this provides the most sensitive results, it takes a longer time to complete than other methods.

- **Madin-Darby Canine Kidney (MDCK) Cell Culture** is different type of additional test used following PCR testing to detect live, infectious virus. This is done by injecting a sample into specific tissue cells to determine whether any live virus is present and replicates. This method can usually be done more quickly than embryonated egg viability studies, but it is not as sensitive and **may provide false negative results when the amount of virus in the sample is very low**.

Precautions for Raw Milk

The FDA has a long-standing recommendation to consumers not to consume raw milk (milk that has not been pasteurized). Because of the limited information available about the possible transmission of H5N1 virus via raw milk, the FDA continues to recommend that industry does not manufacture or sell raw milk or raw milk products, including raw milk cheese, made with milk from cows showing symptoms of illness, including those infected with avian influenza viruses or exposed to those infected with avian influenza viruses.

Importantly, the FDA has also recommended producers take precautions when discarding milk from affected cows so that the discarded milk does not become a source of further spread. Producers should consult with their state regulatory authorities for specific recommendations or requirements; however, such precautions should include heat treatment, pasteurization or its equivalent, of discarded milk prior to dumping in lagoons or application of waste solids and ensuring biosecurity around lagoons (e.g., ensuring that animals and birds do not have access to lagoons). Any raw milk or raw milk products from exposed cattle that are fed to calves (or to other animals, such as farm cats) should be heat treated or pasteurized.

Conclusion

The PMO and pasteurization continue to provide important measures to assure milk safety. Given this is the first time we have seen this virus affect cows, these are the first studies that have been initiated to look at the effectiveness of pasteurization on HPAI viruses such as H5N1 in bovine milk.

As previously noted, the FDA is collaborating closely with CDC's food safety group, as well as its surveillance team that's monitoring emergency department data and flu testing data for any unusual trends in flu-like illness, flu, or conjunctivitis. To date, surveillance systems do not show any unusual trends or activity. Only one associated human case from a person exposed to infected cows has been linked with this outbreak in dairy cows to date and CDC says risk to the general public remains low.

The FDA and USDA are working closely to collect and evaluate additional data and information specific to H5N1 in dairy cattle and to support state counterparts as this emerging disease in dairy cattle is managed. These important efforts are ongoing, and we are committed to sharing results as soon as possible. In the meantime, the FDA and USDA continue to indicate that based on the information we currently have, our commercial milk supply is safe.

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[i] 21 CFR part 131 -- milk and cream. (n.d.). https://www.ecfr.gov/current/title-21/chapter-I/subchapter-B/part-131

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[iii] Jay, J. M., Loessner, M. J., Golden, D. A., & Keller, H. B. (2005). Food Protection with High Temperatures. In Modern Food Microbiology (pp. 415–441). https://link.springer.com/chapter/10.1007/0-387-23413-6_17

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[v] Chmielewski, R. A., Beck, J. R., & Swayne, D. E. (2013). Evaluation of the U.S. Department of Agriculture's egg pasteurization processes on the inactivation of high-pathogenicity avian influenza virus and velogenic Newcastle disease virus in processed egg products. *Journal of Food Protection*, 76(4), 640–645. https://doi.org/10.4315/0362-028x.jfp-12-369

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