

October 14, 2019

Arkansas Department of Health
Center for Health Advancement
4815 W. Markham Street
Little Rock, AR 72205

Re: Draft Rules Pertaining to [Human] Milk Bank Standards

To whom it may concern:

Thank you for the opportunity to comment on the recent proposed rules pertaining to [Human] Milk Bank Standards as authorized by Act 216 of 2019. This Act directs the Department of Health (ADH or the Department) to, “establish, by rule, standards for transporting, processing and distributing commercial human breast milk on a for-profit or nonprofit basis in [Arkansas].”

I am writing as General Manager, Regulatory Affairs at Prolacta Bioscience (Prolacta). Prolacta is the nation’s leading hospital provider of human milk-based nutritional products for fragile infants in the neonatal intensive care unit (NICU). Prolacta’s 100% human milk-based nutritional products are the only way to provide a nutritionally appropriate, exclusive human milk diet (EHMD) to these infants. An EHMD has been clinically proven to improve health outcomes, decrease complications and mortality, and reduce hospital costs when used in replacement of cow milk nutrition in the NICU for babies born weighing less than 1250 grams¹. Prolacta’s main product is a breast milk-derived human milk fortifier, which is mixed with a mother’s own milk or donor milk to provide the most fragile babies an exclusively human milk, nutritionally enriched diet. In Arkansas, our products are currently used at St. Bernard’s Medical Center and Willow Creek Women’s Hospital.

Prolacta is grateful to the Arkansas Legislature and the Department for its leadership in issuing draft guidelines for the regulation of human milk banks. This is a crucial issue. In the last few years, Prolacta has been working with policymakers at both the state and federal levels for thoughtful, comprehensive regulation of this emerging industry. Prolacta believes in the highest standards for milk safety and quality, especially given the population served. Human milk nourishes the most vulnerable members of our society, and we believe that smart regulation gives these infants their best fighting chance for a full and healthy life.

In the absence of stronger oversight at the federal level, Prolacta is happy that states are taking action to ensure that premature infants are not put at risk. For that reason, we were very pleased that the ADH is issuing regulations for human milk banks. However, we are concerned that the draft guidelines do not ensure the safest possible supply of human donor

¹ Abrams, Steven A, et. al. “Greater Mortality and Morbidity in Extremely Preterm Infants Fed a Diet Containing Cow Milk Protein Products.” *Breastfeeding Medicine*, 9, 6. 26 June 2014. Downloaded from: <https://www.liebertpub.com/doi/full/10.1089/bfm.2014.0024>.

milk. Many of the recommended guidelines mitigate some of the biggest risks posed by donor human milk, such as the requirement for pasteurization, a mainstay of bioburden reduction. But the guidelines do not address serious risks that exist in the donor milk supply chain, including traceability of donated milk or screening for contamination by nicotine, opioids or marijuana. Below is a brief discussion of three crucial areas where Prolacta believes these regulations could be significantly improved without significant burden to the Department. These are classification and labeling, testing, and traceability. Each is discussed below.

Classification and Labeling:

Human milk is a unique substance and is therefore difficult to categorize in a regulatory regime. At the federal level, human milk is classified as a food, although specialized formulations of human milk (such as Prolacta's fortifier) are classified as an exempt infant formula, a more highly regulated food. In risk profile, however, human milk closely resembles other donated human tissues like blood or semen. Prolacta believes that each of these approaches has merit, and each presents different obstacles for regulators. For the purposes of Arkansas' proposed regulatory regime, we will focus largely on the FDA's current food regulations.

While many of the Department's proposed milk banking regulations mirror existing federal guidelines, the proposed regulations fall short specifically around safety and labeling requirements. The FDA, in 21 CFR 100-169, requires safety and labeling minimums which are not included in the draft guidelines published by ADH. For example, the draft guidelines do not require milk banks to have a food safety management plan, to adhere to good manufacturing practices (GMPs), or to validate their processes. Prolacta believes that, at a minimum, the ADH's guidelines should meet the FDA's standards for human milk as a food or infant formula. In addition, the FDA's Grade A Pasteurized Milk Ordinance, which establishes standards for processing cow's milk to be consumed by individuals at much lower health risk than premature infants, has a stricter set of guidelines than the state's draft guidelines. We believe that matching and enforcing these requirements is incumbent on the state, especially when donor milk products are being used to feed such a vulnerable population.

As noted, donor human milk is currently regulated as a food at the federal level. However, donor milk is widely recognized to be the second choice for feeding low birth weight infants behind mother's own milk. This is because all donor milk distributed via donor milk banks is pasteurized. While pasteurization is a necessary and required step to reduce the bioburden of human milk, it also alters (albeit safely), the "nutritional composition" and bioactivity of human milk. The change in "nutritional composition" and bioactivity that occurs during donor milk's pasteurization makes donor human milk a partial replacement for mother's own milk which is, according to the Federal Food, Drug and Cosmetic Act, the definition of an exempt infant formula. Therefore, as all donor milk is pasteurized and pasteurization changes the "nutritional composition" of donor milk, relative to mother's own milk -- which is "food" when directly fed to mom's individual

baby, donor milk meets the definition of an exempt infant formula, and arguably should be held to a higher regulatory standard. The FDA's exempt infant formula standards would, in Prolacta's opinion, be a good starting point for further strengthening ADH's regulations.

Finally, it is underappreciated that the nutritional composition of human milk varies between individual women and over time during lactation. These differences, or variability, include components critical to the nutrition of premature newborns such as the milks' caloric, fat, protein and mineral content. However, there are no requirements for labeling the nutritional composition of donor milk in the ADH's draft regulations, despite the fact that the FDA requires labeling of all food and infant formula products, including donor milk.

For that reason, Prolacta believes that the rules established by ADH must include a requirement for basic food labeling for all donor milk and donor milk-derived products. This in turn, would enable the neonatal team caring for an extremely low birth weight and premature infant to administer the proper amount of nutrition, and not just volume of donor milk, meeting the infant's nutritional needs to allow for optimal growth and development.

Testing:

As noted above, human milk is a secreted biologic fluid and hence has the potential to transmit any virus, disease, or pathogen that any other human body fluid, like blood, can transmit. Additionally, premature infants are known to be immune compromised and hence, more likely to develop overwhelming infections resulting in death. For that reason, Prolacta is concerned that the ADH guidelines in their present form, do not address the serious risk of transmission of infectious diseases.

One prominent example is *Bacillus cereus* (BC). *Bacillus cereus* is a bacterium ubiquitous in our environment largely in soil and environmental water, but it is difficult to detect without using a selective and differential method such as those described in the FDA's Bacteriological Analytical Manual. While BC is effectively reduced by pasteurization, the spores it produces are resistant to pasteurization. Under certain conditions, BC can produce an enterotoxin that attacks the gastrointestinal tract causing severe complications. Hence, the germination of BC spores can lead to fatal illness in preterm infants. A literal life-saving requirement that ADH should include is that all donor milk and donor milk-derived products must undergo testing specific for the detection of BC and, potentially, enterotoxins to avoid the bacteria flourishing in the gut of highly vulnerable preterm infants.

In addition to pathogens like BC, human milk is unique in that chemical substances like nicotine, marijuana, and drugs of common abuse can also be passed from the blood stream into breast milk. The ongoing opioid epidemic and the spreading legalization of marijuana pose significant health risks to the donor milk supply. Not only are these substances alone a threat to infants, but earlier this month, the CDC announced that the opioid crisis has quintupled the rate of pregnant women who have been diagnosed with Hepatitis C.

Prolacta believes that all donor milk and donor milk-derived products must be screened for, at a minimum nicotine, amphetamine, benzodiazepine, cocaine, marijuana (THC), methamphetamine, opiates and their principle metabolites. Donor screening, as recommended in the ADH draft guidelines, is not sufficient. The only way to ensure that donor milk is free chemical contaminants and pathogens that transmit disease and is to directly test donor human milk and donor milk-derived products.

Traceability:

In its most recent donor milk guidelines, the American Academy of Pediatrics stated that, “human milk is a biological product; therefore, whether from an infant’s own mother or a donor mother, there will always be concerns about contamination.” Prolacta agrees with this assessment, and therefore, it would be prudent not only for the Department’s guidelines to address the unique risks of biologics included in our recommendations above, but also to ensure the traceability for all commercial human milk banks that collect, process, store, and distribute, in the state.

In recent years, great strides have been made in improving the traceability of the food supply, to the extent that outbreaks of *Salmonella* or *E. coli* can often be traced to contamination from a specific field at a specific farm. The same is not true of the human milk supply. Right now, many milk banks can only assume the milk donated to them came from qualified donors screened for appropriate risk factors. Unlike blood, plasma and tissue, milk is expressed at home by the donor. Mix-ups and errors in the collection process can, and do, happen. Given the high-risk population to whom donor milk is provided, better traceability standards are absolutely needed.

Prolacta therefore strongly encourages the Department to consider an absolute traceability requirement for all donor milk and donor milk-derived products, as is standard for any other biologic or tissue being licensed by the Department, and as is increasingly the norm even for conventional foods.

We again thank the Legislature and the Department for your leadership on this critical issue and would be happy to provide any expertise or data we can to supplement the suggestions offered in the above. Thank you for your commitment to making the donor human milk supply safer for all.

Sincerely,



Scott Eaker
General Manager, Regulatory Affairs
Prolacta Bioscience

August 18, 2020

Arkansas Department of Health
Center for Health Advancement
4815 W. Markham Street
Little Rock, AR 72205

Re: Revised Rules Pertaining to [Human] Milk Bank Standards

To Whom it May Concern:

Thank you for the opportunity to comment on the revised (July 2020) proposed rules pertaining to [Human] Milk Bank Standards as authorized by Act 216 of 2019. This Act directs the Department of Health (ADH or the Department) to “establish, by rule, standards for transporting, processing and distributing commercial human breast milk on a for-profit or nonprofit basis in [Arkansas].”

I am writing as the Chief Operations Officer at Prolacta Bioscience (Prolacta). Prolacta is the nation’s leading hospital provider of human milk-based nutritional products for fragile infants in the neonatal intensive care unit (NICU). Prolacta’s 100% human milk-based nutritional products are the only way to provide a nutritionally appropriate, exclusive human milk diet (EHMD) to these infants. When used as part of an Exclusive Human Milk Diet (EHMD), Prolacta’s products are clinically proven to improve health, reduce complications¹²³, and shorten length of stay⁴ for extremely premature infants in the neonatal intensive care unit (NICU). Prolacta’s main product is a breast milk-derived human milk fortifier, which is mixed with a mother’s own milk or donor milk to provide the most fragile babies an exclusively human milk, nutritionally enriched diet.

Prolacta remains grateful to the Arkansas Legislature and the Department for its leadership in issuing draft guidelines for the regulation of human milk banks and releasing enhanced draft guidelines following the initial public comment period. This is a crucial issue, particularly because there are already numerous milk banks operating in Arkansas and serving the state’s most vulnerable infants. These milk banks include, but are not limited to, milk banks affiliated with the Human Milk Banking Association of North America (HMBANA), Medolac Laboratories, and Prolacta Bioscience. There are also more milk banks on the market, and likely either already operating in or soon to be operating in Arkansas. Prolacta believes that given the vulnerable

¹Abrams, Steven A, et. al. “Greater Mortality and Morbidity in Extremely Preterm Infants Fed a Diet Containing Cow Milk Protein Products.” *Breastfeeding Medicine*, 9, 6. 26 June 2014. Downloaded from:

<https://www.liebertpub.com/doi/full/10.1089/bfm.2014.0024>.

² Critofalo, Elizabeth, A, et al. “Randomized trial of exclusive human milk versus perterm formula diets in extremely premature infants.” *J. Pediatr.*, 163, 6. December 2013. Downloaded from: <https://pubmed.ncbi.nlm.nih.gov/23968744/>

³ Sullivan, S, et al. “An exclusively human milk-based diet is associated with lower rate of necrotizing enterocolitis than a diet of human milk and bovine milk-based products.” *J. Pediatr.* 156, 4. April 2010. Downloaded at: <https://pubmed.ncbi.nlm.nih.gov/20036378/>

⁴ Assad, M, et al. “Decreased cost and improved feeding tolerance in VLBW infants fed an exclusive human milk diet.” *J. Perinatol.* 36, 3. March 2016. Downloaded at: <https://pubmed.ncbi.nlm.nih.gov/26562370/>

population these milk banks are serving; it is imperative that both states and the federal government ensure milk banks comply with the highest standards for milk safety and quality. Human milk nourishes the most vulnerable members of our society, and we believe that smart regulation gives these infants their best fighting chance for a full and healthy life.

For this reason, we were very pleased that the ADH is issuing regulations for human milk banks, and greatly appreciate the Department's expansion of the guidelines, especially including Section 27, Tracking and Recall of Donor Milk, and Sections 4 – 9 regarding donor qualification and screening, exclusion criteria, etc. These are critical elements that we are grateful the Department is taking into consideration.

In response to these revised guidelines and given the delicate and life-and-death implications of these guidelines, on behalf of Prolacta, I ask the Department to consider the following comments on the revised guidelines. These requests are made for two reasons: (1) some to follow the most recent and highest quality guidelines available, and (2) some to ensure that more than one milk bank is permitted to operate in the state. **Since the Department's draft guidelines are primarily, though not entirely, drawn from HMBANA's internal guidelines, there are certain policies included in the guidelines that are unique to the operations of HMBANA-affiliated milk banks, and would prohibit competition in the state that no other state prohibits, as well as effectively eliminate continued access to human milk-based human milk fortifiers currently used in Neonatal Intensive Care Units (NICUs) in the state.** We have provided justifications for each of the requested changes below, and believe that these changes will enhance, rather than degrade, safety and quality of donor human milk, while promoting competition and access to donor human milk.

Accordingly, I have listed below our suggested amendments to these guidelines. I welcome any questions or further discussion on these requests and am happy to make our entire team of regulatory, safety, and quality experts available at your convenience.

Requested Amendments to Drafted Human Milk Bank Rules

- Section 2. Definitions
 - 2.6 – Donor Human Milk. This section refers to donor human milk as milk pasteurized using the Holder Pasteurization Method. We request this is amended to read, “donated by lactating women, ~~pasteurized using the Holder Pasteurization Method~~ **subjected to a validated pathogen inactivation method**, and dispensed...” This change is requested because the Holder Pasteurization method is only one of several bioburden reduction methods approved by the US Food and Drug Administration (FDA). In fact, Holder Pasteurization is not a pasteurization method even recognized by the Pasteurized Milk Ordinance, rather it is a method more commonly used in albumin pasteurization processes. Further, Prolacta and some other milk banks, use alternatives to the Holder Pasteurization method that provide a comparable or better level of pathogen inactivation as the Holder method. Requiring a milk bank to comply with this particular method limits each milk

bank's abilities to utilize a pathogen inactivation method they deem most appropriate for their products.

- 2.6.3 – Similarly, we request that this section is titled, “Bioburden Reduced Milk”, and that the specifics of the Holder Pasteurization are replaced to read as follows, “fresh-raw and/or fresh-frozen milk that has been ~~heated to 62.5 degrees Celsius, for 30 minutes~~ subjected to a validated method of pathogen reduction.”
 - 2.11 – Milk Donor – This definition refers to, “a lactating woman who voluntarily contributes milk to a human milk bank.” We are concerned over the use and ambiguity of the term, “voluntarily.” Some milk banks remunerate donors for their milk, and some do not. Act 216 of 2019 requires the state to regulate and license all milk banks and makes no mention of remuneration received by donors. We fear that use of the term voluntary could create confusion over this issue, and, without intention, either omit regulation of milk banks that do provide remuneration to their milk donors or prohibit donors from being remunerated for their milk. We request that the definition is amended to read as follows, “A lactating woman who voluntarily contributes milk to a human milk bank. ~~A donor may or may not be remunerated.~~”
 - 2.12 – Milk Processing Centers – We believe this subsection should be omitted from the rules. This is a definition that non-profit milk banks use within their own guidelines, but is irrelevant in government regulations, especially those being promulgated by the state of Arkansas, since Act 216 of 2019 requires the state to, “establish, by rule, standards for transporting, processing and distributing commercial human breast milk on a for-profit or nonprofit basis in [Arkansas].” Prolacta believes that all milk banks – for-profit, non-profit, and otherwise – are included under subsection 2.5 – Donor Human Milk Bank.
- Section 3. Administrative Structure
 - 3.1 – A Medical Director plays a key role within the milk bank, particularly as it relates to ensuring safety and quality protocols are consistently reviewed and strictly followed. As such, we request the term Medical Director is added within the Administrative Structure.
 - Section 4 – Donor Qualifications/Screening
 - 4.2 – This section prohibits milk banks from solely using electronic forms of communication with donors. While we understand the intent of the language is to ensure that close, personal communication is established with donors, in Prolacta's experience, electronic communication is preferred by many new mothers because it is less time intensive and can be addressed at a mother's leisure. As currently written, this subsection would adversely impact those donors who prefer electronic communication without providing any evidence as to why alternative forms of communication are inherently superior. Using electronic communication in no way prevents milk banks from ensuring the donor receives the required serological tests of complies with any safety guidelines, nor does it impact the milk bank's ability to secure all required medical information from the donor's physician, etc. At Prolacta, we test every single batch of milk received down to the DNA to ensure it

matches the qualified donor. We are confident that regardless of the form of communication our milk bank has with the donor, the milk we use for our products is safe, and our donors receive ample and constant communication. Prolacta requests that the subsection be amended as followed, “Screening ~~must~~ may include in-person, ~~or~~ on-the-phone, or electronic contact, ~~and must never be limited to electronic communication.~~”

- 4.4.1 – For the same reasons listed above, we request this subsection is amended to read as follows, “They have been screened verbally ~~and~~ or in writing...”
- 4.4.3 – Since the serological tests used by most milk banks to qualify donors provide a snapshot in time as to the health of a prospective donor rather than a guarantee of their continued suitability to donate, milk banks should have a protocol in place for requalifying donors in order to ensure their continued eligibility. We have suggested language for a requalification process further in this letter. In addition to the inclusion of this language, we suggest this subsection is amended to address the requalification process by reading, “A CLIA certified high complexity clinical laboratory or an ISO 17025 accredited clinical laboratory does the tests, and results are valid throughout the time of donation, ~~and until the donor is requalified,~~ unless life-style or medical issues suggest an increased risk for donation, in which case deferral or resting is at the discretion of the individual milk bank.
 - 4.4.3.1 – Donor communication varies based on the donor and the milk bank. We suggest that the requirement for communication intervals is left to the milk bank to determine, so long as they milk bank is performing direct testing of milk, which allows the milk bank to ensure safe and quality milk in every batch. We request the rules under 4.4.3.1. are amended to read as follows, “communication with a milk donor regarding her health and lifestyle is expected ~~to be no less than every 90 days and documented in the donor’s record~~ occur on a regular basis, so long as they milk bank is performing direct testing of milk for communicable diseases received from the donor. In the absence of direct testing of donated milk, communication with a milk donor regarding her health and lifestyle is expected to be no less than every 90 days and documented in the donor’s record.”
- 4.4.4 – At Prolacta, we have an in-house, full-time Medical Director who reviews medications, viruses, and bacteria of concern constantly. This allows for more immediate and thorough reactions to threats but understand not every milk bank has the same structure. We therefore request that this section takes this into consideration, and is amended as follows, “reviewed by the Members of the Medications Committee at least annually, ~~or on an ongoing basis by the Medical Director,~~...”
- 4.4.4.5 – As currently structured, this section describes a specific list of drugs that are permissible for prospective donors to take. Prolacta believes that many drugs are safe for a nursing mother to take while donating, but that these decisions are best left to the Medicines Committee or Medical Director of a milk bank, based on adherence to evolving CDC and FDA guidelines. Therefore, we suggest that the

this section be amended as follows, “Prospective donors taking medications that ~~include are limited to~~ the following list do not need deferral”.

- Section 6 – Exclusion Criteria
 - 6.10 – Prolacta believes this subsection is redundant with some of the language covered in more detail in section 4.4.4 (and its subsections), and to a lesser extent, section 5. In addition, there are a number of allowable daily medications that Prolacta has found (and other sections of the draft guidelines confirm) do not have an impact on donor suitability; ranging from birth control to stool softeners. For example, 4.4.4.5.4 allows for daily use of non-sedating antihistamines, but subsection 6.10, as drafted, would appear to require the exclusion of such a donor for taking an over-the-counter medication.
 - 6.12 – The milk donated from vegans who do not supplement their diet with vitamin B12 can be a risk only if the milk bank does not test the final product to ensure adequate levels of protein are present in the donor milk or donor milk derived product. This capability, used by some milk banks, ensures all processed milk meets minimum nutritional standards, and negates the need to exclude donors who are total vegetarians/vegans. Accordingly, we suggest this subsection is amended to read as follows, “total vegetarians (vegans) who do not supplement their diet with the vitamin B12, **unless the milk bank conducts macro-nutritional testing with results showing that each batch contains a minimum of at least 0.9g/dL of protein.**”
- Section 7 – Temporary Disqualification
 - 7.2.7 – At Prolacta, we require a donor to be deferred following receipt of a tattoo as a result of potential risk associated with the use of needles used for the creation of the tattoo. However, we believe the requirement to defer a donor based on their partner’s receipt of a tattoo is unnecessary and over burdensome as there is no risk to the donor if they were not in direct contact with needles. Even blood bank guidelines do not require donor deferral due to a partner receiving a tattoo.
- Section 8 – Serological Tests
 - 8.1 – There is a conflicting guidance in subsection 4.4.3 and 8.1 with regard to serological screening for HIV-1 and -2, HTLV-1 and -2, Hepatitis C, Hepatitis B, and syphilis. Subsection 4.4.3 states that the screening must be done “no more than 6 months prior to the first donation,” while subsection 8.1 states that the screening must be completed “within 6 months prior to a woman’s becoming a donor.” Since many milk banks qualify new donors months in advance of receiving their first donation, we would like to ensure this requirement is consistent throughout the guidelines. We suggest the addition of “donation date,” under Section 2 – Definitions (see suggested definition further down) to address this issue, and clarity and consistency throughout the rules that serological screening is conducted within 6 months of the donor being qualified.
- Section 9 – Donor Approval

- We suggest the same changes in donor communications requirements as we have suggested under section 4.4.3,1. that communications,” **occur on a regular basis, so long as they milk bank is performing direct testing of milk received from the donor. In the absence of direct testing of donated milk, communication with a milk donor regarding her health and lifestyle is expected to be no less than every 90 days and documented in the donor’s record.”**
- Section 11 – Donor Education and Procedures
 - 11.2 – In this subsection, we would simply ask for clarity that “written instructions” includes electronic, written instructions.
- Section 12 – Procedure Manual
 - At Prolacta, we constantly review and revise all of our quality and safety measures. A full review of our procedures manual, however, is conducted every two years, per the FDA’s guidelines, as well as other states that regulate and license milk banks. These draft rules, however, require an annual review. We suggest these rules are adjusted to reflect the FDA’s requirements for a full review of the procedures manual every two years.
- Section 14 – Equipment
 - We suggest updating the title of this section to “Equipment within the Milk Bank.” As currently drafted, this section is confusing because it is not clear whether the thermometers, freezers/refrigerators, etc. referenced are those of the milk bank or donors. We believe that renaming the section will add clarity. Further in this letter, we also provide suggestions for regulations surrounding the donor’s freezer as well.
- Section 15 – Thermometers
 - 15.3.2 – In order to cover various thermometers and freezers used by milk banks, we suggest the following revisions to subsection 15.3.2, “Thermometers **or temperature recording devices should may be certified** calibrated by **using standards traceable to the** National Institute of Standards and Technology (NIST) (or similar agency) or **similar based on the frequency (quarterly, bi-annually, or annually) as required by regulation or recommended by the manufacturer of the walk-in freezer. calibrated quarterly by the milk bank using an NIST-certified reference thermometer.** The milk bank must keep records of calibration.”
- Section 17 – Thermometer Calibration Procedure
 - We believe this section is already addressed under subsection 15.3.2. We therefore recommend it be removed.
- Section 23 – Aliquoting and Heat Processing
 - 23.1-Aliquoting. This section is directed to safety steps a milk bank must take when using Holder pasteurization methods. For milk banks that do not use Holder pasteurization, aliquoting prior to bioburden reduction is not necessary. As such,

we request this section only apply to those milk banks performing Holder pasteurization.

- 23.2 (and subsections 23.2.1 – 23.2.2.2) – Heat Processing. Similar to the points made under subsection 2.6, the procedure required for heat processing in this subsection limits the state’s ability to regulate any pathogen inactivation process that does not include the Holder pasteurization method. Some milk banks, for example, may prefer to use the Vat pasteurization method, and some use retort processing. We believe that any and all of these processes should be overseen by ADH. We suggest that to accomplish this task, the subsection 23.2 (and subsections 23.2.1 – 23.2.2.2) is replaced with the following:

A milk bank must create a validated procedure for the reduction of viral and other pathogens in human milk-based products. For example, pasteurization is the process of heating a particle of milk in a properly designed and operated equipment to a specific temperature and held continuously for a definite length of time as defined by the “Pasteurized Milk Ordinance,” and provides one means for effectively reducing bioburden when performed correctly and in accordance with the guidance provided in the Pasteurized Milk Ordinance.

Additionally, the final product shall be tested for the presence of microbial organisms, and acceptable limits for those organisms shall established.

The testing procedure shall be representative of the entire production run, and the amount of product tested shall be sufficient to detect the number of organisms allowed per the release specification.

- 23.4.1 – Labeling of Milk. We agree wholeheartedly that labeling is a critical component to distributing safe milk. However, common practice is to base the expiration date off of the date the milk has been pasteurized, not when it was expressed. In addition, Prolacta has over a decade of data that has been accepted by the FDA regarding the stability of our product for two years from date of pasteurization. We therefore request that this subsection is amended to read as follows, “containers are labeled with batch number and expiration date of not more than ~~1 year from the earliest pumping date of milk in pool from~~ 2 years from the date of pasteurization.” We further suggest that the expiration date is based, not on a fixed time period, but rather on product stability data collected over time by the manufacturer.

23.6.1 – This subsection requires milk banks to have, “the microbiology Standards of Practice (SOP) available in their banks, distributed by Human Milk Bank Association of North America (HMBANA). Individual milk banks ensure that the microbiology lab performing the Standards of Practice from HMBANA available in their milk banks and ensuring the compliance with the microbiology lab performing the testing is in compliance with the procedures.” We are concerned about this requirement, as HMBANA is one of several milk banks that operates in Arkansas and throughout the country, and believe it is inappropriate for the rules

set forth by the state for all milk banks to comply with the SOPs put forth by another milk bank. Instead, we suggest the rules require compliance with the FDA's Bacteriological Analytical Manual (BAM).

- Section 26 – Milk Bank Records
 - 26.1.2 – In line with the comments made re. subsection 8.1, we would like for the serology testing to be consistent throughout the guidelines.
 - 26.1.4 – We suggest that this is amended to read, “Birth date and gestational age **or date of birth** of donor’s infant.” for streamlined compliance and coordination with healthcare provider records.
- Section 27 – Tracking and Recall of Donor Milk
 - 27.1 – We are emphatically supportive of the addition of the tracking and recall section to these draft rules. We cannot stress enough the importance these two items have on ensuring a safe donor milk supply is maintained and delivered to babies. However, we are concerned with the vague description of the tracking system outline in 27.1, and suggest, that section 27.1 is amended to read something along the lines of the following,

“Unlike blood, plasma, or other tissues, donation (expression) of milk does not occur in a specific location under the direct observation of organization personnel. Rather, potential donors pump milk at home or a location convenient for them and later deliver that milk to the operation. Consequently, it is incumbent upon each organization to determine the method that it will use to ensure that the milk received at the organization originated with the donor whom the organization has screened and qualified. This is particularly important for operations that do not directly test human milk and instead rely only on the questionnaire and blood test of the donor to assess risk of exposure.

- The method shall be applied to every donation received from every donor.
 - The method shall provide reasonable certainty that the milk contained in the donation originated from that individual, and that only that individual’s milk is in the donation.
 - In accordance with GMP, and in certain jurisdictions, Good Tissue Practice (GTP), discovery that a donation contains milk from more than a single donor or contains milk that is not from the original donor, shall trigger an internal investigation. This may result in the permanent deferral of the donor involved.
 - Final product will be affixed with a marking *e.g.* barcode that identifies the lot from which the product was made, and the individual donors who contributed to that lot. Records shall be kept indicating where each barcoded product is shipped for use.”
- 27.2 - We emphatically support the addition of proof that a milk bank is able to recall a product, as well. However, we are concerned that a 6-hour period for a mock recall is not possible for any milk bank to comply. Further, we believe that

adverse event reporting is key to any recall process. Therefore, we suggest the following language replace the current language in subsection 27.2,

Adverse Event Reporting and Product Complaint

The organization shall establish a process for handling, investigating, and responding to product complaints and reported adverse events for any written, oral comment, or allegation regarding concern or dissatisfaction for possible health hazards, appearance, taste, odor, or other matters of quality. This shall include a standardized reporting process that includes basic information regarding the complainant, affected product details, and details regarding the issue reported. The process shall be communicated to customers, so they are aware of the complaint process. When appropriate, the process shall document a prompt assessment regarding the potential hazard to health. It shall also establish an escalation process to the appropriate regulatory authorities when issues are identified that indicate there is a potential for product that has been misbranded, adulterated, or potential risk to human health. The complaints handling process shall also provide a mechanism for using the complaint as an opportunity and good practice for learning and improvement, when possible.

Requested Additions to Drafted Human Milk Bank Rules

- Section 2. Definitions
 - Donation Date – the date on which the milk bank receives the milk donation, whether the donation is made in person, by mail, or otherwise.
 - Expression Date – the date on which the donor expresses her milk
 - Medical Director- A milk bank shall have a medical director who is a licensed physician with a minimum of four years of experience in neonatology, pediatrics, blood banking, infectious disease, or a related field.
- Section 4. Donor Qualifications/Screening

We believe it would be helpful for the rules to include guidelines on the donor requalification process. Our suggested language for this process is as follows,

“Donor Requalification

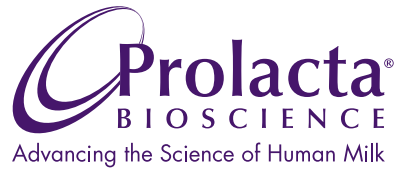
The qualification process provides a snapshot of the donor at the time the qualification process was performed. In order to provide an updated assurance of donor suitability, a requalification process shall be put in place by the organization for donors who wish to continue donating after a certain point following their initial qualification.

Milk banks must requalify donors at a maximum interval of every 6 months.

- We also believe that enhanced screening and testing ensures the safest milk supply possible. In addition to the requirements included in Section 4, we propose the following additional requirements:
 - Physician Attestations

A statement from the donor's primary care physician is required, attesting to the best of their knowledge, the donor's general good health and the lack of any contraindications to donation.

In the case of milk donation, the donor's own child may be affected if the donor's supply is limited or if the donor opts to donate all their milk and feed their own baby(ies) artificially. Therefore, a statement from the pediatrician or medical provider responsible for the baby's care is required, attesting to the good health and growth of the baby, and that the baby is being exclusively breast-fed (at least until the baby is 6 months of age). This does not apply to a donor who is not responsible for feeding her own baby for medical or legitimate social reasons (e.g. a baby with breast milk allergy or infant demise).
 - Testing of Milk Donations for infectious disease and adulterants
 - Regardless of whether blood testing is used as an initial screening method for infectious disease, direct testing of milk donations for the presence of nucleic acid of specific pathogens shall be performed.
 - Pathogens present below the threshold of detection would be present in amounts orders of magnitude lower than the ability of heat treatment at 63°C for 15 minutes to deactivate.
 - At a minimum, the test panel shall contain the same pathogens tested for in blood tests. The test must be validated and properly controlled, organizations may, at their discretion, add additional pathogens to their testing regimen if the medical director or Medical Advisory Board believe it will improve the safety of the milk supply.
 - An organization may choose to eliminate blood testing of donors as being redundant only after the tests have been properly validated and the Department is satisfied the direct test of milk is suitable replacement for blood testing.
 - In addition to direct testing of milk donations shall also be done to ensure the milk is free of common adulterants including nicotine, cocaine, opiates, opioids, benzodiazepines, and amphetamine (or relevant metabolite). The organization may conduct these tests by any validated method including but not limited to ELISA-based assays.
 - At the milk bank's discretion, additional adulterants may be added to their testing regimen, if in the opinion of the medical director or Medical Advisory Board doing so will improve the safety of the milk supply and therefore the safety to its recipient.
 - The Medical Advisory Board will meet at least annually to review the panel of pathogens and adulterants being tested and recommend additions when warranted.



- The donor will be accepted or deferred based on the screening test. However, in the event of a positive screening test, a confirmatory test may be obtained by the organization for informational purposes only..

We again thank the Department for its leadership on this critical issue and would be happy to provide any expertise or data we can to supplement the suggestions offered in the above. Thank you for your commitment to making the donor human milk supply safer for all.

Sincerely,

A handwritten signature in black ink, appearing to read 'Scott Eaker', with a long horizontal line extending to the right.

Scott Eaker
Chief Operations Officer
Prolacta Bioscience



August 19, 2020

Laura Shue
General Counsel
Arkansas Department of Health
Center for Health Advancement, Public Health Laboratory
4815 W. Markham Street
Little Rock, AR 72205

Arkansas Board of Health Rules Pertaining to Milk Bank Standards

Dear Ms. Shue,

We appreciate the opportunity to provide comments directed to the Board of Health Rules Pertaining to Milk Bank Standards. Specifically, we write regarding laboratory testing and calibration requirements and the related laboratory accreditation standards.

By way of background, A2LA is a non-profit, accreditation body with over 3750 actively accredited certificates representing all 50 states and international, including 27 organizations accredited in Arkansas. We have been granting accreditation to laboratories in various industries since 1979. The criteria forming the basis for our testing and calibration laboratory accreditation programs is ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories. We also provide accreditation to clinical laboratories to ISO 15189 Medical laboratories – Requirements for quality and competence, and to the Centers for Medicare and Medicaid Services (CMS) Clinical Laboratory Improvement Amendments (CLIA) requirements.

We ourselves, as an accreditation body, have been evaluated against rigorous standards in providing these accreditation services and we are the only accreditation body in the world that is recognized globally as an International Laboratory Accreditation Cooperation (ILAC)-recognized accreditation body and CMS deemed status accreditation organization.

We offer the following comments specific to the use of the ISO/IEC 17025 standard for medical testing and calibration. The recommended language is inserted in **bold**:

In section 4.4.3, the requirements specify “A CLIA certified high complexity clinical laboratory or an ISO 17025 accredited clinical laboratory does the tests...” Please note that an ISO standard exists that is based on ISO/IEC 17025 and ISO 9001 but specifies requirements for quality and competence that are particular to medical laboratories. This ISO standard is ISO 15189 and has been in use for close to twenty years.

We recommend that 4.4.3 be revised to **“A CLIA certified high complexity clinical laboratory or an ISO 15189 accredited clinical laboratory, that achieved accreditation from an International Laboratory Accreditation Cooperation recognized accreditation body, does the tests...”**

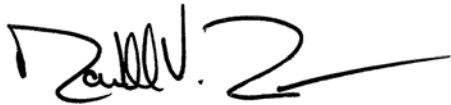
In section 15.3.2, the requirements specify, "Thermometers may be certified calibrated by National Institute of Standards and Technology(NIST) (or similar agency), or calibrated quarterly by the milk bank using an NIST certified reference thermometer. The milk bank must keep records of calibration."

It is industry practice to rely on NIST calibration or rely on an ISO/IEC 17025 accredited calibration laboratory that is accredited by an ILAC recognized accreditation body for calibration of the reference thermometers. Then the milk bank may verify working thermometers against the reference thermometers.

We recommend the following revision to section 15.3.2: "Thermometers may be calibrated by a national metrology institute (NMI) such as the National Institute of Standards and Technology (NIST) or an ISO/IEC 17025 accredited calibration laboratory that is accredited by an ILAC recognized accreditation body, for the calibration of the reference thermometers. The milk bank shall verify working thermometers against the calibrated reference thermometers at least quarterly. The milk bank must keep records of the calibration and verification records."

If you have any questions about ISO/IEC 17025, ISO 15189 or laboratory accreditation, please feel free to contact me at my direct line (301) 644-3221 or via email at rquery@A2LA.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Randall Querry", followed by a long horizontal flourish.

Randall Querry
Director Government Relations
American Association for Laboratory Accreditation (A2LA)