FDA Working Group
Backgrounder on
Banked Human Milk

I. PURPOSE FOR THIS MEETING

FDA is convening this meeting to obtain a better understanding of Human Milk Banking--current practices, infectious disease risks, state regulations and mitigation strategies currently used to avoid contamination of donated milk. The Agency has been involved in both internal and external discussions regarding issues associated with the distribution of banked human milk. At this point in time, the Agency decided to hold a Pediatric Advisory Committee (PAC) meeting to gather more information on the subject and invite experts to speak and discuss the topic. In addition, in the Federal Register announcement, FDA asked the public to speak at the Open Public Hearing session of the PAC meeting agenda and also submit information to the open public docket. The information gathered in these various scenarios will be used in future deliberations and available to the public on our website.

II. INTRODUCTION

The benefits of human milk from healthy mothers to their infants are well established. The immune system of the mother provides antibodies against pathogens; this immunity is passed through the breast milk to the infant's gastrointestinal tract. Other benefits of breast milk include its nutrient composition and various bioactive components that are protective to the infant. Human milk has been associated with reduced morbidity and mortality from gastrointestinal, respiratory, and other diseases.

However, human milk can be a source of infection or adverse exposures to nursing infants, including maternal-infant transmission of viral infections (e.g., CMV, HIV); intrinsic chemical contamination of the human milk (such as from certain pharmaceuticals and certain environmental contaminants); and bacterial contamination. Generally, these risks can be more easily identified and controlled in the context of direct mother/child breastfeeding

A network of human (also referred to here as "donor") milk banks has developed since the mid-1980s, primarily in the United States. These banks, described more fully below, pool, process, and distribute donated breast milk from lactating women for use in other infants when the mother's own milk is unavailable. Most of these banks voluntarily follow a set of guidelines established by the Human Milk Banking Association of America (HMBANA: HMBANA's "Guidelines for the Establishment and Operation of a Donor Human Milk Bank—2009"). More recently, FDA became aware of a large scale human milk company, Prolacta Bioscience, Inc. (Prolacta) which has begun processing and distributing certain human milk-based products for profit. Finally, there appears to be a market for distribution of breast milk through Internet transactions, although the extent of this market is unknown.

The risks associated with banked human milk may be donor-derived, introduced during handling and processing, or related to whether or not the nutritional needs of the infant are met.

The purpose for this meeting is to discuss the issues associated with human milk banking and some of the following issues:

- What are the risks related to consumption of banked human milk and how do these risks vary among the sources and processing of the milk?
- What voluntary or regulatory controls currently in place mitigate these risks?
- What additional scientific research might be needed to further advance our knowledge concerning the risks?

III. BACKGROUND

Sources of human milk

HMBANA has been in existence since 1985. According to its website, HMBANA is "a multidisciplinary group of health care providers that promotes, protects, and supports donor milk banking." HMBANA, which is the only professional membership association for human milk banks, sets standards and guidelines for donor milk banking including protocols for its members that include donor screening, pasteurization, and post-pasteurization testing. Participation in HMBANA is voluntary, as is adherence to the HMBANA guidelines.

HMBANA's website states that there are eleven HMBANA member milk banks providing human donor milk to the US and Canada. In 2000 the banks dispensed a combined total of 409,077 ounces of milk. That rose to 745,329 ounces of milk in 2005—a 45% increase. In 2005 the HMBANA milk banks distributed milk to hospitals in over 80 cities located in 29 states and 3 Canadian provinces.

Another source of donor milk and donor milk products is Prolacta Bioscience. Prolacta is a for-profit company that manufactures products made from donated human milk including two pasteurized human milk products not containing added minerals or processing beyond pasteurization; a pasteurized human milk-based product with added minerals; and a human milk fortifier containing added minerals that undergoes additional processing (ultrafiltration) to concentrate the product.

Prolacta's website states that they provide a fortifier made from 100% human milk and that their products are distributed in NICUs across the country.

State Regulatory Oversight

The HMBANA guidelines are formally recognized (through legislative action) as the standard for human milk banking by the states of California and Texas. New York has its own statutory authority over donor milk banks either operating or distributing donor milk within the state. Only these three states have statutory oversight of donor milk banking, although Florida and Maryland require licensure for the operation of donor milk banks.

Food Good Manufacturing Practices (GMPs)

Current food Good Manufacturing Practices (GMPs) are published in Title 21 of the Code of Federal Regulations Part 110 (21 CFR 110). GMPs describe the methods, equipment, facilities, and controls for producing processed food. As the minimum sanitary and processing requirements for producing safe and wholesome food, they are an important part of regulatory control over the safety of the nation's food supply. GMPs also serve as one basis for FDA inspections.

Risks associated with donated human milk

Donated human milk may be contaminated with bacteria, viruses, or chemicals (e.g., pharmaceuticals, environmental) intrinsically at the time of collection, or extrinsically during collection, processing, or storage. Consideration should be given to the risks associated with exposure to any of these substances. There may also be nutritional factors that need to be addressed. What is less clear is the extent to which the risks associated with donated human milk that has been collected, processed and distributed in accordance with the milk establishment protocols (HMBANA and Prolacta) are mitigated by compliance with those protocols. The extent to which risks are known to be mitigated is discussed in each section below.

Infectious disease transmission risks

Human milk can transmit bacteria, viruses, fungi or parasites either from the donor (maternal transmission), or because of contamination with infectious disease agents after collection.

There are multiple methods, used by HMBANA banks as well as by Prolacta, by which infectious disease risks may be mitigated:

- Donor screening and testing measures are focused on identifying and excluding donors who are at risk of transmitting certain infectious disease agents (e.g. viruses and syphilis).
- Self-exclusion, based upon information provided by the milk establishment to the donors, is used to decrease the risk of maternal bacterial transmission. For example, donors are asked not to collect donations during times when they are febrile, have warm and/or red breasts, or feel ill.
- There is an effort to minimize contamination of the milk by the donors through educational materials explaining clean techniques for milk collection (washing and sterilizing pump parts, hand washing, appropriate containers in which to collect and store milk, proper handling of containers), labeling of donated milk, procedures for freezing and storing milk, and procedures for transporting milk to the bank.
- Milk bank storage and handling procedures are designed to minimize the risk of contamination of milk at the milk bank.
- Heat processing is done by the Holder method in HMBANA banks. This method can legally be used to pasteurize cow's milk (the primary method of pasteurization used for cow's milk is High Temperature Short Time—161^0F for 15-20 seconds) and will kill or inactivate many infectious disease agents but

neither the Holder method nor the High Temperature Short Time method is a sterilization procedure.

There are uncertainties related to infectious disease transmission from banked human milk in the United States. There are no data to show there have been direct infectious disease transmissions from banked human donor milk within the United States. Compliance with the protocols recommended by HMBANA or used by Prolacta will mitigate the infectious disease risks from banked donated human milk, but it is not clear the extent to which residual risk remains.

If the human milk donor pool has a high risk for infection, the concerns regarding the potential for missing infectious diseases because of donor screening and testing procedures would be increased. This certainly raises the concern for testing protocols that may miss window period infections. The processing (pasteurization) likely addresses many of the infectious disease risks, but likely not all of them.

Non-infectious contaminants

HMBANA and Prolacta screening procedures include questions about some personal practices of donors that could result in the presence of non-infectious contaminants in pasteurized, banked milk (e.g., , intake of prescription drugs, over-the-counter drugs, herbal products, tobacco products, alcohol, and recreational drugs). Neither HMBANA nor Prolacta assesses the donated human milk for these types of contaminants by testing.

Nutritional Considerations

Infants have different nutritional needs at different stages of development and health status. Donated human milk varies in composition because during the course of lactation most nutritional components decline in concentration during the first few months (particularly protein, sodium, zinc and copper, with lactose remaining fairly constant). Human milk donated to milk banks is usually from mothers who have given birth to term infants and have well-established milk production.

Quantitative and qualitative changes occur when human milk undergoes collection, storage, and processing before feeding. Although heat treatment of human milk destroys microorganisms, it also results in reduced nitrogen retention and fat absorption (because of human milk lipase destruction) by infants. Concentration of certain water soluble vitamins is also reduced.

Term human milk may not be adequate for the specific nutritional needs of premature or certain critically ill infants. Preterm infants have different nutritional requirements than the full term infant because of the greater immaturity of multiple organ systems. Infants born prematurely are not a homogenous group and depending on the gestational age and condition of the infant, their nutritional requirements will vary. Failure to meet these increased nutritional needs can have profound effects on somatic growth, structural and functional development of organs, particularly of the brain. Preterm infants require more energy, protein, vitamins and minerals to meet the goal of mimicking intrauterine growth accretion of energy and protein. The nutrient content of human milk, regardless of its source (either banked milk or a mother's own milk fed directly to her infant), is inadequate in energy, protein, vitamins and minerals to meet the growth requirements of preterm infants.

Although the nutritional needs of preterm/medically compromised infants are not met by human milk alone, the use of human milk is often part of the strategy to ready the preterm infant's gut to better accept future enteral feeds and provide the preterm infant the protective components of

their mother's milk. Preterm infants receive a combination of parenteral and enteral feedings until they are able to accept enteral feedings alone. Progression of feedings depends on clinical conditions and feeding tolerances. Human milk, when available, is usually fortified to better meet the calorie, protein, vitamin and mineral needs of the preterm infant. Few data are available to assess whether feeding banked human milk provides similar outcomes to direct feeding of milk from a mother to her infant.

The nutritional considerations for term versus preterm infants are not addressed under the HMBANA guidelines. The individual nutritional needs for pre-term and medically compromised infants are beyond the scope of this discussion; that issue is addressed for individual infants as part of medical practice.

Benefits associated with donated human milk

The nutrient content of human milk is designed to meet term infants' growth needs. In addition, many of the nutrients have multiple functions. For example: lactoferrin, a major human milk protein also provides iron in a bioavailable form to the infant and promotes anti-bacterial protection in the infant's gastrointestinal tract. The role of human milk glycans (complex carbohydrate structures) is to act as a protective component. These indigestible carbohydrates contain non-reducing termini that resemble the human intestinal receptors that cause pathogens to bind to these termini and protect the infant from diarrhea associated with various pathogens.

Recently, benefits associated with the long term programming effects from human milk fed directly from mother to her infant in early infancy have been proposed and include possible reduction of later cardiovascular health disease, type II diabetes, blood pressure and obesity. It is not known if donated banked human milk would provide such purported benefits.

The American Academy of Pediatrics 2005 policy statement, "Breastfeeding and the Use of Human Milk" states:

> Banked human milk may be a suitable feeding alternative for infants whose mothers are unable or unwilling to provide their own milk. Human milk banks in North America adhere to national guidelines for quality control of screening and testing of donors and pasteurize all milk before distribution. Fresh human milk from unscreened donors is not recommended because of the risk of transmission of infectious agents.[1]

IV. Other Considerations

Unlike other regulated products involving living human donors (e.g., blood, cells, tissues), banked human milk is collected and initially stored without direct medical or manufacturer (milk bank) intervention in the donor's home; these unique collection and storage circumstances raise novel and difficult questions concerning the appropriate regulatory oversight (e.g., application of regulations, donor testing, inspection, recalls, and enforcement) related to donor human milk.

[1]Pediatrics 2005; 115: 496-506