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## NeoLacta Lifesciences – Ensuring an Exclusive Human Milk Diet for Pre-term Infants through Donor Human Milk-Derived Nutrition

Dr. Vikram Reddy K.

MBBD, MD, Chief Scientific Officer (CSO)

[drvikram@neolacta.com](mailto:drvikram@neolacta.com)

NeoLacta Lifesciences Pvt Ltd, Bengaluru, Karnataka

### ABSTRACT

*Each year 15 million premature babies are born globally of which ~ 1.1 million don't survive beyond a few weeks. Almost 3.5 million babies are born prematurely in India alone, the highest globally for any nation. For such prematurely born babies, the mother's own milk is the best source of nutrition. Human breast milk provides optimal nutrition, reduces the risk of NEC and Sepsis, builds immunity, strengthens the gut flora, and supports neurocognitive development. Numerous clinical trials have proven the value of human milk and products derived from human milk, especially for the sick and vulnerable premature population. Screened and pasteurized human milk has been the recommended option by healthcare bodies globally when a mother's own milk is unavailable. Donation of surplus milk from healthy nursing mothers can make a world of difference by proving to be a lifesaver for premature babies and their families. Donating milk also brings a sense of satisfaction to the donor mother since her milk will benefit many other babies along with her own. Besides, it also promotes the well-being of the donor mother by reducing the risk of conditions such as engorgement and mastitis. A healthy nursing mother with excess breast milk should consider donating it to the sick and premature babies thereby contributing to building a healthier next generation. The endeavor is to draw the attention of the reader toward the importance of human milk donation and its impact on the health and well-being of premature babies. Through this white paper, NeoLacta Lifesciences would also like to highlight the safety, robustness, and ethicality of its operations. Our objective is to create a resilient framework by bringing together all stakeholders – healthcare professionals, parents, family, community, and policymakers towards destigmatizing this noble initiative of human milk donation.*

**Keywords**— Neolacta, MMF, PHBM, Human Milk Donation, Preterm

### 1. INTRODUCTION

This white paper will explore the need for the donor human milk-derived nutritional products for the preterm infants and the health benefit attained from the exclusive human milk diet. The incidents of preterm birth are a global problem; however, the WHO 2018-19 data shows that more than 60% of preterm births occur in Africa and South Asia. On average, 12% of babies are born prematurely in lower-income countries as compared to 9% in higher-income countries. Within a country, poorer families are at a higher risk. The survival of premature babies also depends on where they are born; almost 9 out of every 10 preterm babies in high-income countries survive because of enhanced primary care and awareness, in low-income countries this number is 1 out of 10.<sup>1,2</sup> An estimated 3.5 million infants are born prematurely every year in India. The NMR (neonatal mortality rate) in India is estimated to be 28 per 1000 live births.<sup>3</sup> Risks associated with Preterm infants- Respiratory distress syndrome, Sepsis and Necrotizing enterocolitis, Intraventricular hemorrhage and periventricular leukomalacia

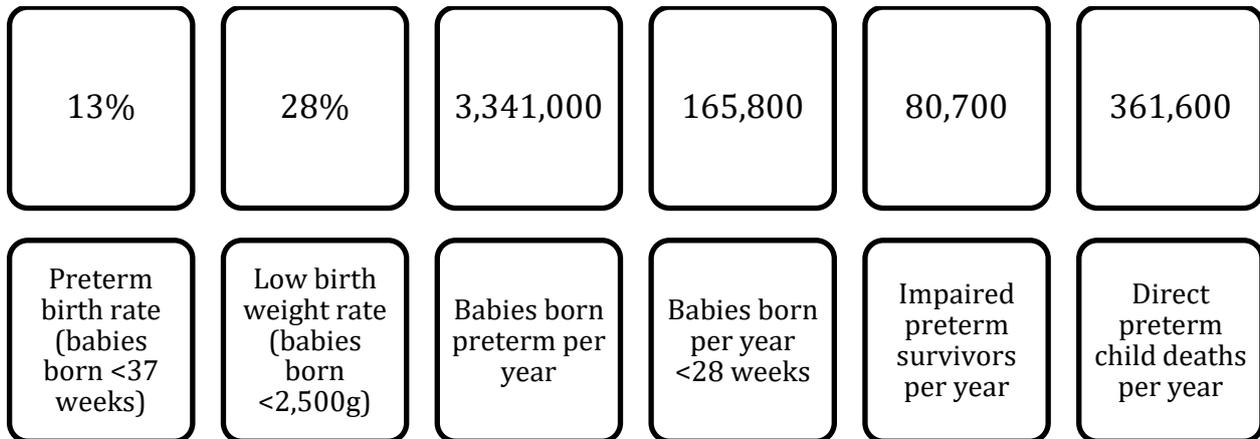
Human breast milk is the best form of enteral nutrition for preterm new-borns. The milk could be from the infant's mother or donor mothers, i.e. mothers who have delivered full-term infants. The nutrient content of expressed breast milk depends on the stage of lactation at which it is collected. Donated drip breast milk may not consistently provide all of the nutrient requirements of preterm infants. Multi-nutrient fortifiers like calcium phosphates are sometimes added to human milk to increase human milk protein and energy supplementation.

Human breast milk also has significant non-nutrient advantages for preterm infants. The primary benefit is the delivery of immune-protective and growth factors to the immature gut mucosa. Certain evidence proves that preterm infants who receive human breast

milk rather than formula milk have a lower incidence of feed intolerance or gastrointestinal problems and a lower incidence of necrotising enterocolitis (usually fatal).<sup>4,5</sup>

## 2. PRETERM STATISTICS IN INDIA

In India 3,341,000 babies are born prematurely each year and 361,600 children under five of age die due to direct preterm complications.<sup>6</sup>



Short-term benefits of exclusive human milk feeding for the baby:

- Breast milk is a rich source of lactose and essential fatty acids that help a baby's brain development.
- Breast milk regulates healthy bacteria in the baby's gut
- Human milk feeding decreases the incidence and severity of infectious diseases like bacterial meningitis, diarrhoea, respiratory tract infections, necrotizing enterocolitis, otitis media, urinary tract infection, and late-onset sepsis in preterm infants. In addition, post-neonatal infant mortality rates are significantly decreased.
- Breastfeeding encourages skin-to-skin contact and nurturing, enabling to soothe and comfort the infant.
- In premature infants, several studies show a positive relationship between the quantity of breast milk received during hospitalization and neurodevelopment.<sup>7</sup>

Long-term benefits of exclusive human milk feeding for the baby:

- Babies who are breastfed have a reduced risk of obesity, diabetes mellitus, lymphoma, leukemia, hypercholesterolemia, and asthma in adulthood.
- Studies have reported that breastfed infants show enhanced performance on tests of cognitive development, especially if breastfed exclusively and for a more extended period of time.
- Breastfed premature children had better psychomotor development at 2 to 5 years than non-breastfed children.

Human milk is chemically and physically a complex biofluid containing relatively high amounts of lipids and carbohydrates and numerous living cells and organisms. Due to these complexities, human-milk analysis has been challenging, requiring adjustments in sample pre-processing and assay validation and optimization.

About 75% of premature infants can be saved with appropriate and cost-effective interventions. These include kangaroo mother care, prompt neonatal resuscitation, timely detection and treatment of neonatal infections and breastfeeding. Of these, breastfeeding has been identified as the single most powerful method, with the potential to prevent 0.16 million under-5 deaths in India. Yet the data shows that breastfeeding rates remain low, with only 41.6% of infants being initiated into breastfeeding within 1 hour of birth and 54.9% of infants exclusively breastfed until six months of age.

### 2.1 Neolact product studies

Neolact is the only company in India and Asia dedicated to improving access to Human Milk through their products fully derived from Human Milk. These products aim to address the needs of neonatal nutrition, thereby playing a critical role in ensuring "intact survival" for premature babies.

Various clinical trials have proven the value of human milk-derived products in saving lives of premature babies and low birth weight babies (< 2500g). It acts as an effective substitute for low / non-lactating mothers.

Some of these products and their related studies are shown below-

### 3. CASE STUDY: DR ANICE JOY, CONSULTANT NEONATOLOGIST, KOCHI<sup>8</sup>

This case demonstrates the positive effect of Human milk-derived fortifier (*Neolact MMF*) in a preterm baby having an intolerance to bovine milk-based fortifiers. a case report of cows milk protein allergy (CMPA) in a girl baby born at 30 weeks gestation weighing 1500 gm, admitted in NICU with birth asphyxia and severe respiratory distress syndrome (RDS), Fortification with a bovine milk-based fortifier (BMBF) was initiated at 100 ml/kg/day feeding volume, baby developed severe feed intolerance episodes and the mean weight gain was 5 g/day, due to which, fortification was switched to a different brand of BMBF, baby continued to have feed intolerance in the form of bilious vomiting, significant gastric residual volume (GRV) and abdominal distension after the addition

of BMBF. A probable diagnosis of Cow's Milk Protein Allergy (CMPA) was made and the baby was put on human milk-based fortifier (HMBF), CMPA was mitigated by switching to HMBF (NeoLact MMF), which resulted in cessation of feed intolerance and providing an effective weight gain (30 g/day). HMBF can be considered as a safe and effective fortification option for preterm infants.

#### **4. EARLY FORTIFICATION STUDY WITH NEOLACT MMF – Dr. Manesha P et al. <sup>9</sup>**

This single-center pilot study was carried out on five neonates (three males and two females). The neonates were enrolled between June and October 2019. Only those exclusively breastfed neonates were chosen to ensure that all enrolled neonates were uniformly fed an EHMD. The neonates born with a low birth weight (between 800g to 1500g) and/ or born at less than 36 weeks of gestational age (GA), with the ability to adhere to a feeding protocol based on the use of mother's own milk (MOM) or pasteurized donor milk (in case of requirement) and whose parents had the intention to give them only Human Milk were enrolled for this study. Neonates with major congenital malformations or intestinal anomaly and/ or those who had received bovine milk-based formula/ fortifier before this study were excluded.

The standard NICU protocol was followed and total parenteral nutrition was started on day 1. It was continued until the neonates could tolerate more than 50% of the daily feed requirement through oral means. Oral feeds were initiated on day 2, and all neonates received MOM, which was supplemented with pasteurized DHM if MOM was unavailable or insufficient. Based on the chief neonatologist's decision, fortified human milk (FHM) was initiated early, depending upon each neonate's nutritional requirements. According to the manufacturer's recommendation, 25mL of MOM was mixed with 1 g of 100% HMDF. This study used Neolact Mother's Milk Fortifier (MMF; Neolacta Lifesciences Pvt Ltd, Bengaluru, Karnataka, India). At the time of discharge, fortified feeds were stopped and those neonates who weighed at least 1.6kg and were breastfeeding adequately or tolerating all feed requirements were discharged.

The primary aim was to record the Feed tolerability, including the adverse events comprising three or more episodes of emesis within 24 hours, abdominal distention exceeding 2 cm or more, or gastric residual volume exceeding 50%. The secondary outcomes measured were the growth parameters, including mean weight gain (g/d), mean length gain (mm/d), and mean gain in head circumference (mm/d) at the end of the study. The feed volume (mL/kg/d) at the start of fortification and the number of days of fortification were also recorded. Until discharge, the total serum proteins were estimated once every week at the discretion of the chief neonatologist.

- A total of 5 neonates were enrolled for the study. Their mean GA was 32.36 weeks ( $\pm$  1.36 weeks) and birth weight was 1086 grams ( $\pm$  173.8 g). The mean feed volume was 52.2 mL/kg/d ( $\pm$  11.75 mL/kg/d).
- No incidents of feed interruptions were reported; the 100% HMDF was well tolerated by all the neonates.
- In this study, the preterm neonates tolerated the EHMD (with MOM or DHM with HMDF) well.
- This study provides a preliminary report on the effects of early fortification with 100% HMDF on the growth of preterm neonates. We observed that early fortification with feed volumes  $<$  55 mL/kg/d resulted in a faster weight gain and faster discharge from the NICU, compared with fortification with higher feed volumes. For a neonate, the reduction in NICU stay by 5 to 10 days means a reduced risk of hospital-acquired infections and reduced medical costs.
- According to a study by Chan et al, the antibacterial activity of HM can be affected by the addition of BMDF, but not by the addition of a HMDF. As observed by Gathwala et al, the mean gain in total serum proteins at the end of 2 weeks with exclusive human breast milk was 0.32 g/dL. After fortification (fortifier + expressed breast milk [EBM]), the mean gain in total serum proteins was 0.66 g/dL, when the fortification with a BMDF was started at 100 mL/kg/d of enteral feed volume.
- In this study, the mean gain in total serum proteins at the end of 2 weeks of fortification (MMF + EBM) was 1.46 g/dL, when fortification was started early at feed volumes  $<$  100 mL/kg/d (mean feed volume was 52 mL/kg/d). This could suggest advantages of early fortification at volumes  $<$  70 mL/kg/d, which offers a good increase in the protein concentration with a reduction in the requirement of NICU stay. However, these results need to be proved further, with a larger study group.
- This study presents preliminary evidence that early fortification with a 100% HMDF provides adequate growth with optimum amounts of proteins in both ELBW and VLBW preterm neonates without compromising the benefits of an EHMD. The results also indicate good feed tolerance with no clinically significant record of adverse events. Although it adds evidence in this field, more research through a larger sample size is required to conclusively prove that an EHMD supplemented with HM-derived fortifiers will boost the ongoing efforts of neonatologists to reduce neonatal morbidity rates by significant percentages.

#### **5. POST-DISCHARGE NEOLACT 70 SUPPLEMENTATION STUDY IN PRETERM INFANTS. Dr Lingaraju S - Department of Neonatology, People Tree at Meenakshi Hospital, Bengaluru<sup>10</sup>**

NeoLact 70 is a newly developed 100% human milk-based nutritional product. This study done on the use of NeoLact 70 is important to assess its effects on feed tolerance and growth in preterm infants. Our results show that an exclusive HMD regimen with NeoLact 70 results in good feed tolerance, reduced feed interruptions, good weight gain and lesser infections. This study was completed after four weeks of usage of NeoLact 70 in the selected sample of infants.

This is an open label, pilot study done on a sample size of 10 infants. The selection criteria for the infants is as follows-

- Infants who are discharged from the hospital
- Infants who were born preterm
- Infants with low birth weight
- Infants who had at least 1 episode of sepsis/infection during the NICU stay
- Infants who had feed intolerance issues during the NICU stay
- Infants who had poor growth during NICU stay
- Infants who had recurrent infections/diarrhea

- Infants receiving vaccination and on formula/mixed feeds

The infants who had major congenital malformations, intestinal anomalies, or other serious disorders were excluded from the study.

### Procedures

Ten infants who fulfilled the inclusion criteria were enrolled in the study. 1.55gms of NeoLact70(1 sachet) was initiated at the time of discharge, to be used afterward at home. NeoLact 70 was used alongside breastfeeding, with a minimum use of three sachets per day. One sachet of NeoLact 70 was mixed in 10 ml of sterile water and was fed to the infant. Neolact70 was used as supplementary immune nutrition in discharged preterm infants who were receiving breastfeeding. The study was continued four weeks from the day of discharge, after which the neonatologist-in-charge determined the feeding regimen for all the infants in the study. The immunoglobulin profile was analysed through the serum sample taken at baseline (before starting Neolact70) and again at the end of the study. Ten infants were enrolled over the three-month study period between September-November 2020. The mean GA and birth weight of the infants were  $33.5 \pm 4.9$  weeks and  $1779.4 \pm 576$ g (mean  $\pm$  SD), respectively. Overall, good growth was observed, with an average weight gain of 30.4 g/day and good IgA increments (38.29% increase from baseline). There was no requirement for antibiotics/pre-probiotics during the study. Feeds were well tolerated, and no adverse events were noticed. There were no re-admissions /OPD visits or other health complaints such as diarrhoea, respiratory infections, or weight gain issues during the supplementation period.

This study observed that immune-nutritional supplementation with a human milk-derived nutrition (like NeoLact70- 1.55 g) would aid in optimal weight gain, along with an increment in immunoglobulins. This supplementation would be of clinical benefit to premature infants discharged from NICU.

### 6. EFFECT OF HUMAN MILK ENRICHED WITH HUMAN MILK-BASED FORTIFIER (HMBF) VERSUS BOVINE MILK-BASED FORTIFIER (BMBF) ON GROWTH AND MORBIDITY AMONG VERY LOW BIRTH WEIGHT (VLBW) INFANTS – A RANDOMIZED CONTROLLED TRIAL <sup>11</sup>

It is a single-centre, open-labelled, randomized controlled trial (RCT) enrolling very low birth weight (VLBW) neonates of less than 34 weeks of gestation weighing between 1,000 and 1,500 g. Infants were randomized to receive either fortifier (HMBF or BMBF) after reaching 100 ml/kg/day of enteral feeds.

Results: A total of 50 infants were enrolled (25 in each arm). Weight gain (21.42 vs. 20.84 g/day,  $p = 0.77$ ) and growth velocity (16.45 vs. 15.85 g/kg/day,  $p = 0.57$ ) were similar in both groups with no statistical difference. Sepsis (relative risk [RR] = 0.6), feed intolerance (RR = 0.57), necrotizing enterocolitis (NEC) (RR = 0.33) and duration of hospital stay (33 vs. 36 days) were better in the HMBF group than in the BMBF group.

Conclusion: Growth velocity was similar in both groups. However, HMBF was well tolerated by neonates with lesser incidence of feed intolerance, NEC, sepsis, and lesser hospital stay duration than in neonates supplemented with BMBF. Given the fewer number of studies, there is a need for well-powered RCTs with a good sample size to fill the knowledge gap.

Summary of the research publications on human milk derived nutrition is provided in the table below:

Study Status	Title	Sample Size	Growth Velocity (g/kg/day)	GA (weeks)	BW (g)	Length of NICU Stay (days)	NEC (# of Episodes)	Product
Published in IJCH – Dec’2021	An open-label, pilot study to evaluate the benefits of using lyophilized human milk-derived nutritional product (NeoLact 70 – 1.55 g) as an immune-nutritional supplement in premature infants discharged from NICU. <sup>10</sup>	10	30.4 g/day	33.5	1779.4	Post-discharge use	0	NeoLact 70
Published in JPNIM – Italian Journal – Nov’2021	Prospective randomized control study (Human Vs Bovine milk-based fortifiers) <sup>11</sup>	50	16.45	30.34 (28-33)	1294.64 (1192-1396)	MMF: 33 BMBF: 36	MMF: 1 BMBF: 3	NeoLact MMF
Published in Journal of Medical Case Reports and Reviews- July’ 2021	Clinical impact of using a human milk-based fortifier in a preterm infant demonstrating intolerance to bovine milk-based fortifiers – a case report. <sup>8</sup>	1	17.68	30	1500	20	0	NeoLact MMF
Published in Journal of Perinatology – India – July 2020	Effect of Early Fortification With 100% Human Milk-Derived Fortifier on Growth of Preterm Neonates: A Pilot Study. <sup>9</sup>	5	13.56	32.36 (30-33)	1086 (890-1320)	28.6	0	NeoLact MMF

Published in Indian Journal of Child Health – Jan’ 2020	Effect of 100% human milk-derived fortifier on growth of premature infants with birth weight of 1000–1500 g. <sup>12</sup>	13	18.37	31.64 (29-33)	1314.62 (1204-1425)	NA	0	NeoLact MMF
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**Gaps between demand and supply of Human Milk Banks in India**

An estimated 27 million children are born every year in India accounting to about 20% of the births globally, 30% of the infants are born with low birthweight (birth weight <2,500 g).<sup>13</sup> An estimated at 3.5 million infants are born prematurely every year in India. Among these infants, about 7.6 lakh infants within the neonatal period and premature birth being the major cause for this mortality rate, which accounts for 35% of all deaths.<sup>14</sup>

**Gaps in access to Human Milk in India**

Human milk is a liquid gold for the new-born infants which play vital part in development and protection of the infant. Human milk is also considered as the single most powerful intervention with a potential to avert 1,60,000 under-5 deaths in India. Hence, it is of at most importance that all infants need to receive human milk during early infancy period.<sup>15</sup>

Overall rate of breastfeeding is extremely low in India,

- Where only 41.6% of new-born infants are receiving human milk feeding within 1 hour of birth.<sup>4</sup>
- Only 54.9% of infants receive exclusively human milk diet till 6 months of age.<sup>15</sup>

**Demand of donor milk and availability (based on the current milk banks)**

Between 2005 to 2015, India had fewer number of human milk banks (n=22), but since past 4 years, the number of milk banks have increased to 50, but even this increase is still inadequate to meet the huge requirement of donor human milk (DHM) for a country which has 27 million births in a year.<sup>16</sup>

**India compared to UK:**

Sl No	Parameter	Brazil	United Kingdom	India
1	Births/year	29,16,240	7,70,000	2,70,00,000
2	Total Milk Banks	214	16	50

Brazil’s decision to increase the number of milk banks is helping to save around 300,000 lives of new-borns per year, Also Brazil’s milk banking system is thought be the vital intervention in decreasing the country’s infant mortality rate by 73% over the past two decades, i.e., from 63.2 per 1,000 births in 1985 to 19.6 in 2013. (<https://news.umich.edu/learning-from-brazil-s-success-with-milk-banks/>). It has been known that 30% to 50% of the new-born infants in NICU require DHM for minimum duration of 5-15 days, while a premature and an LBW baby would have the higher need. A recent survey conducted on human milk banks in India established that 63% milk banks reported gaps between donor milk demand and supply.<sup>17</sup>

**Annual statistics of donors and recipients in participating human milk banks (N=16), 2015-166:**

Variables	Median (Range)	Public sector	Private sector
Number of donors	600 (70-4000)	1938	316
Volume of milk collected (liters)	382 (30-1085)	498	230
Volume of banked milk utilized (liters)	293 (27-1047)	469	174
Number of recipients	500 (80-3993)	1480	261

A study by Sachdeva et al. (2019) attempts to evaluate the existing status of human milk banks in India concerning metrics like infrastructure, human resources, funding mechanisms, operating procedures and quality assurance.<sup>17</sup>

Methods: A questionnaire was administered to 16 out of 22 human milk banks across India operational for more than one year.

**Results**

- Around 69% of the milk banks were in government or charitable hospitals; only 12.5% were set up with government funding.
- 50% of the milk banks had a dedicated technician, and only one milk bank had more than five lactation counsellors.
- Milk was collected primarily from mothers of sick babies and in postnatal care wards of hospitals, followed by pediatric outpatient departments, camps, satellite centers, and homes. 63% of the surveyed milk banks reported gaps between donor milk demand and supply.
- 75% used shaker water bath pasteurizer and cooled the milk manually without monitoring temperature, and 25% pooled milk under the laminar airflow.
- 63% of the milk banks tracked donor to recipient, and none of the milk banks had collected data on early initiation, exclusive breastfeeding or human milk feeding.

Conclusion: This study highlights the gaps of milk banking practices in India, which include inadequate financial support from the government, shortage of key human resources, lack of robust processes and data gaps, and demand-supply gap of donor human milk.

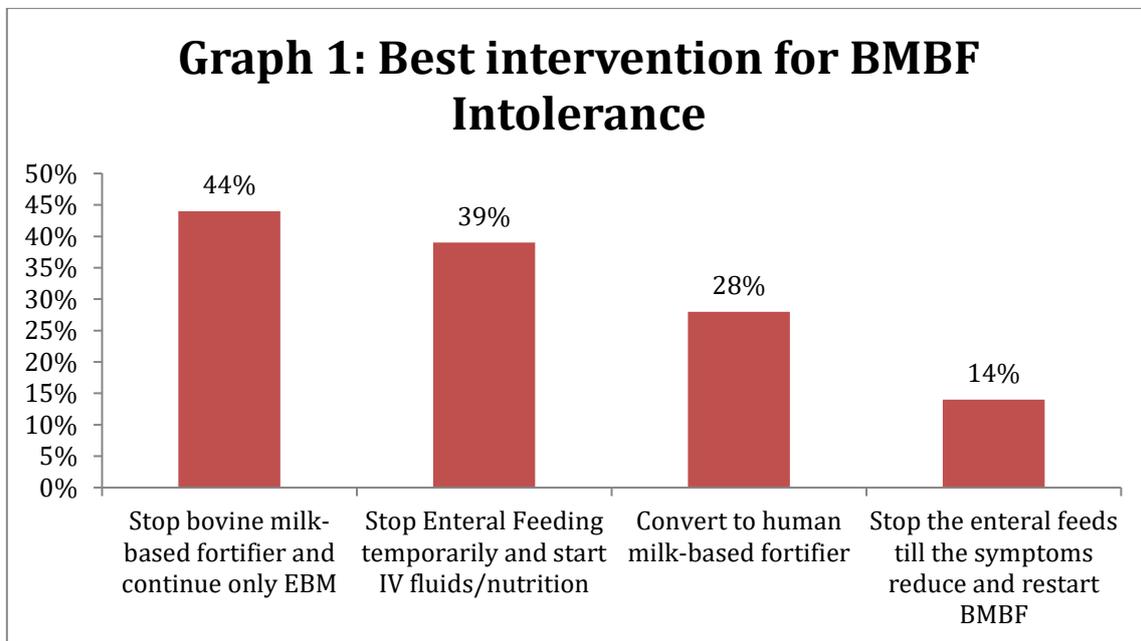
**7. NEONATOLOGISTS SURVEY ON EHMD**

A survey (May to July 2020) of 100 neonatologists across 79 hospitals and 31 cities in India was done to understand the benefits of EHMD (Exclusive human milk diet) from a neonatologist's perspective. A team of researchers designed the survey questionnaire under the supervision of expert neonatologists. The research team analysed the data available on EHMD, preterm enteral feeding protocols, laboratory analysis, and the reports on using donor human milk-based products for premature infants. International and Indian journals were reviewed to study the publications available on this subject; since very few studies are available on this subject matter.

For this study, neonatologists and paediatricians in charge of the NICU and other neonatal care physicians were included, while other speciality physicians were excluded.

**Results**

- All the respondents (100%) agreed that EHMD is important for preterm infants.
- 15% of the respondents opined that EHMD was ensured to all preterm infants, while 80% opined that human milk-based fortifier (HMBF) was safe and well-tolerated by premature infants.
- 40% of the participants reported that around 51-80% of preterm infants receive a BMBF (Bovine milk-based fortifiers in the NICU; whereas 17% of the participants opined that more than 80% of the preterm infants received BMBF.
- On the feed intolerance issues with bovine milk-based fortifiers in NICU, around 17% of respondents reported that 51-80% of the preterm infants on BMBF would experience feed intolerance episodes.
- 44% of the participants confirmed that if feeding intolerance occurs due to BMBF, the best remedy is to stop fortification of feeds and continue only EBM, whereas 28% of the respondents opined that the best option would be to shift over to HMBF (Graph 1).



- 93% of the respondents said that preterm infants would require additional nutritional support after discharge. The details of the responses are given in Table 1.

No. of respondents	Parameters
43	Only mother's own milk
18	Human milk based 70 calorie sachet
31	Human milk based fortifier
7	Bovine milk based fortifier
1	Formula
0	Animal milk

The results from this study highlight the importance of EHMD for preterm infants in NICU. Most neonatologists agree that human milk-derived nutritional products, including HMBF are safe and efficacious. The greater utilization of human milk-based products is also helpful towards the implementation of EHMD in NICU. Further research is needed to confirm and broaden these findings with larger sample size.<sup>18</sup>

**8. NEOLACTA NURSES SURVEY ON EHMD**

As the primary caregivers, NICU nurses play a vital role in the overall management of preterm infants, such as nutrition, feeding and growth measurements for premature infants. Hence, it is crucial to analyse their opinion on the benefits of human milk and

human milk-derived products. This survey's main objective is to understand and analyse the benefits and significance of 100% human milk diet, especially from the NICU nurses' perspective in India.

**Results**

A total of 152 NICU nurses responded to the survey from 81 hospitals across 28 cities in India. Data received from all the completed survey questionnaires were included for further analysis.

1. All participants (100%) agreed that exclusive breastfeeding or using a complete Human Milk Diet is very important for preterm babies in the NICU. None of the participants selected the option of “Not Important”.
2. 97.4% of the participants reported that preterm infants better tolerate feeds if it is a 100% human milk diet; only 2.6% of participants said that a 100% human milk diet is not well-tolerated.
3. 75.7% of participants strongly agreed that the growth of preterm infants is better with a 100% human milk diet.
4. 67.1% of the participants reported that trophic feeds were initiated for preterm infants within 24 hours of birth. All participants opined that the mother's milk is suitable as trophic feeds for preterm infants in the NICU. 44.07% rated that donor human milk is suitable as trophic feeds while 17.76% reported that formula feed is suitable as trophic feeds, and 21.05% of participants have stated that formula feeds cannot be used as trophic feeds.
5. Regarding the feeds for preterm infants in the absence of mother's milk, 46.7% of participants have reported that pasteurized human breast milk, seventy calories (PHBM – 70 calorie), is the best option for preterm infants in NICU.
6. 84.9% of the participants stated that HMDF – Mother’s Milk Fortifier (MMF) is the best option for fortifying breast milk in preterm infants (Table 4).

Table 4: Nurses opinion on the best option for the fortification of breast milk for preterm infants		
	Human milk-based fortifier (MMF)	Bovine milk-based fortifier (HMF)
Nurses’ opinion on the best option for the fortification of breast milk for preterm infants	129	23

7. 96% of the participants reported being satisfied with the safety and tolerance of 100% human milk-based products like PHBM - 70 calorie and HMDF (NeoLact MMF) (Table 5).

Table 5: Safety and Tolerance of 100% human milk-based products like PHBM- 70 calorie and Human milk-based fortifier (MMF) for preterm infants				
	Very satisfied	Satisfied	Neither satisfied nor dissatisfied	Dissatisfied
Nurses’ satisfaction with the Safety and Tolerance of 100% human milk-based products like PHBM - 70 calorie and Human milk-based fortifier (MMF) for preterm infants	65	75	6	0

A large section (84.9%) of the NICU nurses have stated that HMDF - MMF is the best option for the fortification of breast milk, and only a limited number (15.1%) of nurses have opined in favor of bovine milk-based fortifier (HMF). This shows that a 100% human milk diet with human donor milk and its derived products is better than the bovine milk-based products for feeding preterm infants, as per the NICU nurses' opinion.

There is no doubt that the availability of nutritional products derived exclusively from human milk like HMDF (MMF) or NeoLact 70 (in sachet form) has made the implementation of 100% human milk diet possible. This study was carried out on a limited sample size with representations from all the major cities across India but was mostly confined to private institutions. A more extensive study with a larger sample size can provide a more detailed understanding of the NICU nurses' perspectives from both government and private institutions across India.<sup>19</sup>

**9. DONOR’S SURVEY**

This was an independent survey carried out by Aeon Market Research Private Limited, Delhi. Objective of this survey was to understand the human milk donation process undertaken by NeoLacta Lifesciences from donor’s perspective. Survey was conducted using the online survey forms and telephone conversation and the feedback was collated in the survey form.

**Results and Analysis**

- A total of 60 responses were received, out of which an overwhelming 81.7 % said that they used ‘Other’ means (like Google, Facebook, Cloud nine hospitals, and an NGO) to find out about the Breast milk donation process.
- On the question about their decision to donate to Neolacta, 40% of the respondents chose Google as their primary source of information, followed by Facebook (35%), referrals by doctors or close friends, and the use of other social media like WhatsApp chats, etc.
- When asked to rate the Neolacta counselling process on breast milk donation, 56.7% of the responses gave a ‘Very Good’ rating. The counselling session was hugely helpful in clarifying the milk donation process to 68.3% of the respondents. Only about 5% felt that they were still left with some doubts after the counselling process.
- The question on voluntary participation as a donor got a 100% positive response, proving that none were influenced or motivated unjustly.

- The pre-donation serological tests were conducted on around 65% of the respondents, while 35% did not require the tests, as they had the recent test reports (< 6 months).
- A large number of the survey participants, 83.3% to be precise, reported that they had not received any monetary or financial incentives for donating their breast milk, remaining 16.7% reported that they had received support in terms of manual breast pumps. All the participants affirmed that they had donated only excess breast milk.
- About 30% of the respondents had started to donate their milk after the 1st month of delivery, 23% of the mothers after three months, and this number gradually tapered off after six months of delivery. The survey showed that most new mothers prefer to donate their excess breast milk within the first six months of childbirth.
- An overwhelming 93.3% of the respondents confirmed that their baby was normal and healthy during the donation period, remaining respondents had donated due to the demise of the baby. This data affirms that donating excess breast milk does not harm or deprive the donor's baby.
- 59 of the 60 respondents said their doctors were satisfied with their baby's growth and development during the donation period. The only outlier was a baby who had unfortunately passed away during the milk donation period.
- 88.3% of the respondents were exclusively breastfeeding their infants during the donation period, thus proving that the breast milk donation process does not diminish the supply of mother's milk to her infant. Among the respondents who had discontinued exclusive breastfeeding, some of the infants were found to be more than six months of age, hence eligible for an inclusive diet.
- Around 81% of the respondents rated the entire process of breast milk collection as 'Extremely satisfied' or 'Satisfied' (4 or 5 on a scale of 5)
- 58 of the 60 participants found the entire donation experience "very good" or "good."

This survey reaffirms the belief that donating breast milk does not cause any harm to the lactating mother or her child. Other similar global surveys have also established this fact. In addition to being safe, donating breast milk is considered a generous act that brings pride and satisfaction to the donor mothers. This survey will help strengthen our understanding of the current donation process and activate the mechanisms required to improve the donation strategies.

## **10. DONOR ENROLLMENT PROCESS**

When promoting the breast milk donation process, we aim to reach as many potential donors as possible. It is achieved through multiple channels, including:

- Hospitals, including the antenatal clinics and postnatal wards
- Voluntary and other organizations working in areas of maternity and childbirth
- Maternity shops
- Child-care centres
- Recommendations and referrals from current and previous donors, staff at neonatal intensive care units, pediatric clinics
- Through electronic and social media

When conveying written information about the uses of donor milk and donor milk banking, it is imperative to use clear and non-technical language.

### **Screening and selecting donors**

Donor Counselling: Interested donors will be contacted via telephone the trained donor counsellor would counsel the mothers on the process of donation with complete details. With the consent of the potential donor, following questions about the donor's general background and habits would be asked for. For example:

- About her general health
- Document the age and health of her baby
- If she has/had any exposure to consistent passive smoke in her surroundings?
- Is she currently undergoing any medical therapy or taking any medication?
- Is she exposed to sustained levels of environmental or chemical contaminants that can be expressed in breast milk?
- Exposure to any recent infection (including HIV 1 or 2, hepatitis B or C, syphilis, herpes, or acute or chronic infections)
- Exposure to diagnostic radioactive isotopes or any recent medical interventions.

Following the counselling, interested donors would be asked to complete the screening questionnaire form (described below):

## **11. NEOLACTA SCREENING QUESTIONNAIRE FOR MOTHERS**

Neolacta uses a detailed questionnaire to get information about the potential donor mothers and their current health status. Some of the sample questions from the questionnaire are mentioned below-

1. Name of the mother.
2. Her age.
3. Husband's name.
4. Total number of children.
5. Copy of birth order of recent delivery.
6. Age of the recently delivered child.
7. Working status of the mother.
8. Average monthly income of the family.
9. Highest educational qualification of the mother.
10. Dietary Habits (whether Veg/Non-veg).
11. Is she currently breastfeeding?
12. Major illnesses suffered.

13. General Health status.
14. Details of the regular medications taken (prenatal vitamins, insulin, thyroid medications, nasal sprays, inhalers, birth control pills, etc.)
15. Recent blood tests and their reports:
  - Anti-HIV Ag/Ab
  - HBsAg
  - Anti HCV
  - Syphilis/VDRL
  - Anti HBc Total
16. Other serological tests.
17. Willingness to undergo more tests (at the cost of the company).
18. Does the mother have excess milk after feeding her infant?
19. Does she consume illegal drugs/ alcohol/ any form of tobacco/ three caffeinated drinks per day?
20. Is her husband suffering from any of the mentioned diseases-HIV, HBsAg, HCV or Syphilis?
21. Has the potential donor received organ or tissue transport/ blood transfusion/ blood product within the prior 12 months?
22. Is she on radioactive or any other drugs/has chemical environmental exposure/taking over the counter prescriptions/megadoses of vitamins – which are toxic to neonates and excreted in breast milk?
23. Ask mother and assess her breast for mastitis/fungal infection of the nipple or areola? If necessary, observe and assess?
24. Ask mother for active herpes simplex/ varicella zoster infection in the mammary or thoracic region
25. Did she receive any vaccines for Measles, Mumps, Rubella in the last 2 months?
26. Did she receive any vaccines for chickenpox, rotavirus, polio and typhoid in the last 3 months?
27. Is she on any herbs or fenugreek or any other lactation herb to increase milk supply?

## **12. CONSENT**

Before accepting a donor's milk, it is necessary for her consent for the processing and intended use of the donated milk. NeoLacta has a detailed Information sheet and Consent-form for the mothers, which mentions the benefits of breast milk donation and the involved process. The mothers are made aware that their participation is a voluntary one, which can be withdrawn at any time, based on their needs. They are also informed that the breast milk donation activity does not entitle them to receive any payment or favours from any organization or government schemes. The potential donors are encouraged to discuss with their families/ husband before giving their consent.

### **Serological testing**

Serological testing is mandatory for all potential donors to reduce the risk of passing on infections. The potential donor should give informed consent before testing.

Potential donors who test positive for the following should be excluded-

- HBV
- HCV
- HIV (I/II)
- Syphilis (VDRL)

The serological test results are shared with the potential donors.

### **Training and supporting donors**

Fundamental training for all donors covering the following:

- Importance of handwashing
- Good personal hygiene
- Process of collecting and expressing milk, including sterilizing all equipment like breast pumps and containers
- Storing donated milk under proper conditions, including cooling and freezing

It is necessary to provide ongoing support to all donors according to their individual needs, including:

- Information on milk bank requirements
- Continued support for collecting expressed milk and maintaining lactation
- Ongoing support regarding their diet and alcohol consumption

Emotional support and guidance.

## **13. COLLECTION**

Once the screening process is completed which includes, counselling, screening questionnaire, written informed consent, health of both mother and child, and sample for laboratory tests. After successfully completing this step, If the donor is in hospital, the donor is sent to the milk bank's designated breast milk collection area. If donor mother is at home, a donor kit containing labelled collection bottles and a manual breast pump would be sent to donor mother's house. Washing the breast with water or disinfectant before expressing milk is necessary, and it is not required to discard the foremilk. The breast milk expressed by the donor would be stored in the freezer in home or hospital and this would be collected and labelled by trained staff under hygienic conditions and transported to the NeoLacta's plant at Bengaluru under cold-chain management system for further analysis and processing. Only the excess breast milk is collected from the donors. The entire donation process is voluntary and donor mothers will not be paid and there will not be any financial assistance provided by NeoLacta.

### **Collection and Processing at Neolacta**

Neolacta identifies potential donors through hospitals and community outreach. Potential donors are given individual counselling and awareness programs. The breast milk donors for Neolacta are selected after receiving the consent form and going through an extensive screening questionnaire which includes questions about their lifestyle and history of infectious diseases.

The donors are chosen from among healthy, lactating women who:

- Have sufficient lactation to donate after feeding her own baby satisfactorily
- Not taking hazardous drugs
- Not on regular medications that can have an adverse effect on babies, like chemotherapy agents
- Willing to undergo blood tests for screening of infections

Lactating women who pass the pre-approval testing are then screened for a number of diseases that could be transmitted through breast milk like:

- HIV 1 & 2
- HBV (Hepatitis B)
- HCV (Hepatitis C)
- Syphilis

A lactating woman is not approved to be a donor if she has -

- Tested positive for HIV, Hepatitis B or C or syphilis
- A sexual partner suffering from HBV, HIV, HCV and/ or venereal diseases
- Taking radioactive medications and/ or mega doses of vitamins
- Uses illegal drugs and/ or alcohol or more than three caffeinated drinks per day
- Mastitis/fungal infection of the nipple or areola
- Active herpes simplex/varicella-zoster infections in the mammary/thoracic region

Donors who pass the triple screening process are selected for breast milk donation. A breast pump collects breast milk from approved donors, which is later transported through a cold chain.

The bottles are labeled and sealed, frozen to -10°C and transported to the processing area using a cold chain vehicle. The collected breast milk is stored in a deep freezer room at -20°C until it needs to be removed for further processing.

## **14. DONOR MILK PROCESSING**

### **Processing**

The donor milk undergoes pasteurization (Holder's method). At Neolacta, the loss of nutrients from donor milk is minimized by utilizing Australian-developed breast milk processing technologies. The pasteurization process complies with WHO technical guidelines. The Neolacta processing environment comprises ISO-7 and ISO-8 cleanrooms, which comply with FDA GMP guidelines. After pasteurization, the milk is stored in frozen conditions at -20°C, until it is ready for distribution. The pasteurized milk goes through nutritional and microbial testing procedures in internal and external third-party NABL accredited laboratories. No product is released for sale unless it achieves zero microbial growth.

### **Quality and Safety at NeoLacta**

Neolacta Lifesciences located at Bangalore, is the first company in India and Asia to develop an advanced human milk processing facility. This milk facility complies with the guidelines of HMBANA (Human Milk Banking Association of North America) and the FDA pasteurizing standards. It is also ISO 22000:2005 certified, GMP compliant. All the proprietary equipment has been designed and built in Australia by their in-house engineering team to ensure the highest levels of safety and hygiene. Neolacta uses ISO Level 7 and 8 cleanrooms with HEPA filtration and standalone Air Handling Unit (AHU) which comply with FDA GMP guidelines. Batch-specific nutritional information is also provided. The 10 steps described below are followed for each batch of human milk before it is considered ready for distribution

### **Cost effectiveness**

The cost of processing donor breast milk is negligible compared to the medical cost of treating a single case of necrotizing enterocolitis (NEC). Even a small drop in GI complications with the increased use of human breast milk could recover the operation costs of milk banking. Studies support the cost-effectiveness of using donor human breast milk by reducing the length of hospital stay, sepsis and NEC in sick newborns.

An assured benefit is that donor milk banks play a dominant role in increasing breastfeeding awareness in the community, thus, conferring wider benefits to the population.



## 15. NEOLACTA'S INNOVATION IN HUMAN MILK-BASED PRODUCTS

### 1. NeoLacta PHBM 70:

NeoLacta PHBM 70 is pasteurised human milk with the minimum guaranteed energy of 70 cal/100 ml. The product provides essential calories, fat and protein sourced from 100% Human Milk to meet the nutritional requirement of a baby. NeoLacta PHBM 70 can be used when mother's own milk is not available, or the baby needs extra calories for growth. Available frozen in 15 ml and 50 ml bottles.

- Minimum guaranteed energy of 70 cal/100 mL.
- The best source of fat calories to increase the caloric density of human milk diet.
- Provides calorie-dense nutrition without compromising on feed volumes.
- Proteins and immunoglobulins from 100% human milk.

Indication: To be used when mother's own milk is not available, can be used for both trophic feeding and nutritional feeding purposes.

## 2. NeoLact 70 (1.55 g sachet)

Each sachet of NeoLact 70 contains 1.55 g human milk for reconstitution with boiled and cooled drinking water. This product provides minimum 70 kcal/100 ml along with essential proteins and lipids to meet the nutritional requirements of a premature baby. NeoLact 70 can be used when mother's own milk is not available, or the baby needs extra calories for growth. Available in pack of 10 sachets.

- Optimised calorific density without compromising feed volumes.
- Natural source of LCPUFA.
- Retains Immunoglobulins and HMOs.
- Zero maltodextrin (starch) and no synthetic additives.
- Shelf stable at room temperature.

Indication:

- a) Can be used as nutritional feeds when mother's own milk is insufficient or not available.
- b) Can be used as post-discharge immune-nutritional supplement for preterm infants.

## 3. NeoLact MMF (Mother's Milk Factor)

NeoLact MMF (Human Milk Factor) is made exclusively from

100% donor human milk. It provides essential proteins and calories to meet the unique nutritional requirement of a premature baby and most importantly aids in better growth. Available in sachets of 0.5 gm and 1 gm.

- Helps meet protein requirement for premature babies.
- Provides multiple benefits unique to human Milk such as:-
  - Immunoglobulins
  - Human Milk oligosaccharides
  - Lactoferrins
- Offer significant protection against NEC, Sepsis and other complications of prematurity
- Maltodextrin-free ensures excellent feed tolerance when compared to bovine milk-based HMFs.

Mixing Guidelines:

- Mix 1 gm sachet with 25 mL mother's milk; For higher volume feeds use multiples of mixing guidelines.
- Mix 0.5 gm sachet with 12.5 mL mother's milk; For higher volume feeds use multiples of mixing guidelines.

Usage Guidelines:

Pour the recommended volume of breast milk into a sterile container. Add the entire contents of the sachet into the container. Stir well to ensure powder is completely dissolved before feeding. Make a note of the time of feed preparation. Use the feed within 8 hours of preparation. If excess feed is leftover, keep in NICU temperature (22 to 26 degrees) and use within 8 hours. Do not store either the sachets / mixed feed in the refrigerator.

## 4. NeoLact MMF PLUS (Mother's Milk Factor for babies with higher nutritional needs)

NeoLact MMF PLUS (Mother's Milk Factor) is made exclusively from 100% human milk. It provides higher proteins and calories to meet the unique nutritional requirements of babies with specific conditions. Available in sachets of 0.5 gm and 1 gm. MMF PLUS provides 2.2 times higher Proteins to help meet these enhanced nutritional needs.

Special Indication:

Preterm infants with:

- Broncho-pulmonary Dysplasia
- Cardiac anomalies
- Refractory Weight gain

Preparation and usage are similar to of NeoLact MMF.

## 5. NeoLacta PHBM Powder

NeoLacta PHBM is standardised and pasteurised human milk in a powder form. Each 6 gm bottle contains the equivalent of 50 ml human milk when prepared as per instructions. The product provides essential calories, fat and protein sourced from 100% Human Milk to meet the nutritional requirements of a baby. NeoLacta PHBM can be used when mother's own milk is not available or as a supplement to breastfeeding which ensure the baby remains on exclusive human milk feeds. Available as pack of 6 X 6 gm bottles. Standardised and pasteurised human milk powder for reconstitution with water.

Usage Guidelines:

- Wash hands and sterilise all feeding containers.
- Boil drinking water and allow to cool till it reaches lukewarm temperature.
- Open NeoLacta PHBM 6 g bottle and pour 50 ml water up to the indicator line marked on the bottle.
- Close the bottle and mix well to ensure powder is dissolved completely.
- Transfer the mixed feed into a sterile feeding container and cool the feed before feeding.
  
- Discard leftover feed, if any.

### **Commercial Operations:**

Major operational costs include the costs form cold chain transport system, manpower including skilled professionals, research and development including conduct of clinical studies and product testing. The details of the operational costs and various parameters has been described below:

#### 1. Donor awareness programs

- a) Donation awareness initiatives: education and awareness programs.

- b) Content creation
  - c) Website management
  - d) Manpower: digital content manager, graphic designer and donor counsellors.
2. Infrastructure
- a) Deep freezers
  - b) Cleanrooms with Hazard Analysis and Critical Control Points (HACCP)
  - c) Microbiology Laboratory
  - d) Pasteurization and freezing equipment's
  - e) Other equipment: air filters, Generator with UPS.
  - f) Manpower: Quality analysis team, Production Team, Microbiology testing team.
3. Cold chain management system: from collection to plant and from plant to pan-India coverage.
4. Research and Development:
- a) Clinical studies
  - b) Medical affairs
  - c) Product development and testing

## 16. SUMMARY AND CONCLUSION

NeoLacta Lifesciences Pvt Ltd, the pioneer in providing access to human milk-based nutrition in India is empowering the concept of exclusive human milk diet in NICU for premature infants. NeoLacta is able to provide the innovative quality human milk-based nutritional products including the standardised donor human milk and human milk-derived fortifier which will impact the young lives. These products aim to address the needs of neonatal nutrition, thereby playing a critical role in ensuring "intact survival" for premature babies.

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