

# Milk contains NanoVehicles; NanoPrime Labs offers dairy-free NanoVehicles

Dr. Petro P. Czupiel, PhD

## *Abstract*

NanoVehicles are defined as nanostructured vehicles with dimensions ranging from 1 nanometer to 15,000 nanometers. Milk contains two types of NanoVehicles: emulsions and micelles. Emulsions are milk fat globules with diameters between 1,000 and 15,000 nanometers, while casein micelles have diameters between 154 and 230 nanometers. The dominant milk NanoVehicle is dynamically changing and not constant. These two types of milk NanoVehicles are complex, safe-to-ingest, and provide nutrition. Similar to milk NanoVehicles, nanoemulsions and microemulsions are safe-to-ingest mixtures of oil and water stabilized with amphiphilic emulsifiers. Micelles are similar to microemulsions, but without oil. In contrast, dairy-free NanoVehicles are bioengineered to be simpler and smaller in diameter. Nanoemulsions are currently used in cancer treatment and COVID-19 vaccinations, among other uses, and have impactful benefits for treating patients and building immune systems. Unlike nanoemulsions, other dairy-free NanoVehicles are bioengineered to be prepared in the stomach and stomach acid. These NanoVehicles can be loaded with multiple therapeutics and natural health ingredients to achieve enhanced delivery into the blood. Importantly, dairy-free NanoVehicles have the potential to be a highly impactful technology for maximizing the delivery of natural health ingredients into the blood. NanoPrime Labs holds the technology to incorporate oil-loving natural health ingredients into dairy-free NanoVehicles, benefiting consumers' wellness and health.

## 1. Introduction

Milk from humans, cows, goats, and sheep has been a staple in the human diet for at least 10,000 years, with widespread use in Europe, the Middle East, Africa, and Asia since the Neolithic revolution around 8,000 years ago.<sup>1</sup> Milk has consistently provided us with essential nutrition and remains a vital component of modern civilization. In our previous white paper, we explored the distinction between water-loving and oil-loving ingredients. However, milk presents a complex case, as it contains various components that make it challenging to identify the dominant molecules. This white paper will delve into the NanoVehicular technologies present in all milk, including organic milk, shedding light on its intricate composition.

## 2. Milk is a combination of NanoVehicles

Milk is a combination of NanoVehicles, which

are defined as nanostructured vehicles with dimensions ranging from 1 nanometer to 15,000 nanometers. To put this into perspective, one nanometer is one-billionth of a meter, equivalent to the size of a marble compared to the Earth. The NanoVehicles in milk are specifically labeled as emulsions, as milk contains both oil-loving and water-loving ingredients. These milk NanoVehicles are a mixture of two immiscible liquids, oil and water, and consist of two main components: fat globules and milk proteins (**Figure 1**).

The image of milk in **Figure 1(A)** shows its appearance to the naked eye, while **Figure 1(B)** reveals a 1,000x magnified view of the large milk NanoVehicles, or milk fat globules, present in milk. These NanoVehicles make up 95% of milk fat and range in size from 1,000 to 15,000 nanometers.<sup>2</sup> To put this into perspective, 1 nanometer is one million times smaller than 1 millimeter. The opacity and white color of milk are due to the large milk



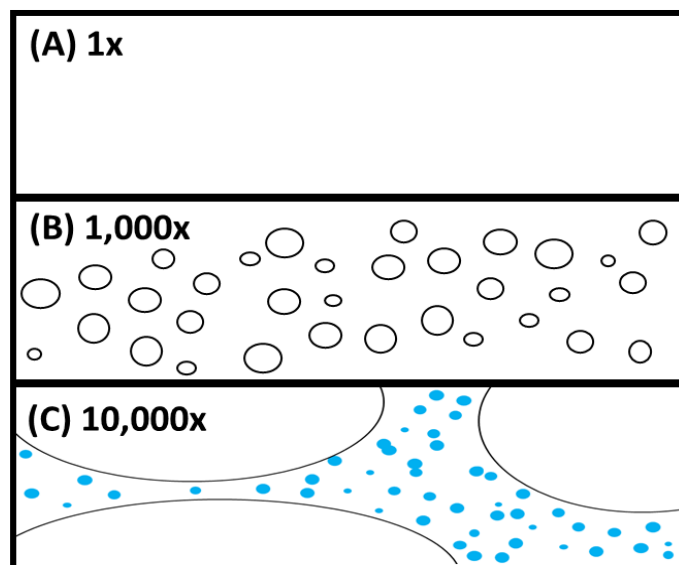
NanoVehicles, which prevent visible light from passing through.

**Figure 1(C)** shows a 10,000x magnified view of milk, with the fat globules surrounded by many milk proteins, including caseins. Caseins are not soluble in water but exist in milk as NanoVehicles with diameters ranging from 154 to 230 nanometers.<sup>3</sup> These casein NanoVehicles are also known as casein micelles, which are the other type of milk NanoVehicle. Therefore, milk is a combination of NanoVehicles, including casein micelles and milk emulsions, or milk fat globules.

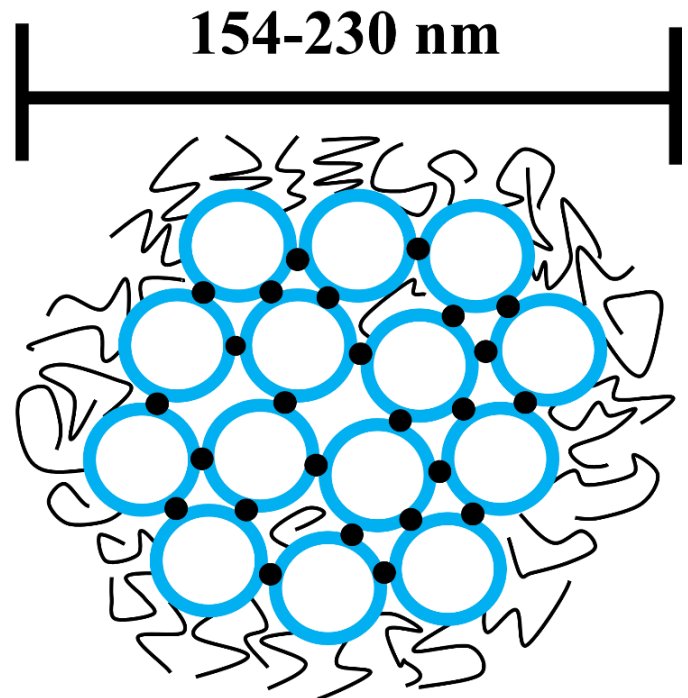
### 3. Milk NanoVehicle 1: Milk Casein Micelles

The complexity of milk NanoVehicles is revealed by examining the smaller milk NanoVehicle, casein micelles, shown in **Figure 1(C)**. A closer look at the casein micelle in **Figure 2** reveals its intricate structure, comprising casein submicelles (blue circles), calcium phosphate nanoclusters (black dots), and chains of proteins (black lines) dangling inside and outside the micelle. Casein micelles are composed of casein submicelles, which are made up of casein proteins that provide amino acids, carbohydrates, and essential elements like calcium and phosphorus.<sup>4</sup>

Casein proteins are further classified into alpha(s1) [ $\alpha$ s1], alpha(s2) [ $\alpha$ s2]-caseins, beta[ $\beta$ ]-casein, and kappa[ $\kappa$ ]-casein, and belong to the phosphoprotein family. They make up 80% of the proteins in cow's milk and 20-45% of the protein in human breast milk, carrying more than half of the protein found in cow's milk.<sup>5</sup> Notably, the protein required by newborn babies is provided by these smaller milk NanoVehicles. The primary function of casein micelles is to carry calcium phosphate nanoclusters, which are complex structures that can bind to various casein proteins.



**Figure 1.** Schematic diagrams of milk with (A) no magnification or 1x zoom, (B) 1,000x magnified image of milk with many large milk NanoVehicles, otherwise known as milk fat globules, and (C) 10,000x magnified image of milk with the other smaller milk NanoVehicles, otherwise known as casein micelles and shown as blue circles, between the three milk fat globules.



**Figure 2.** Schematic diagram representing the various components of the other type of milk NanoVehicle, otherwise known as casein micelles. This type of milk NanoVehicle is made up of casein submicelles, shown as blue circles, calcium phosphate nanoclusters, shown as black circles, and

In summary, milk NanoVehicles, including casein micelles, carry a significant amount of protein found in milk and are safe for consumption by both adults and newborn babies. Their intricate structure and functionality highlight the complexity and importance of milk NanoVehicles in human nutrition.

#### 4. NanoVehicle 2: Milk Fat Globules

The larger milk NanoVehicle, the milk fat globule, exhibits even greater complexity than the smaller casein micelle. Milk fat globules, also known as emulsions or liposomes, are covered by a thin membrane called the milk fat globule membrane (MFGM) (**Figure 3**). The MFGM is analogous to a wall, comprising three layers with a

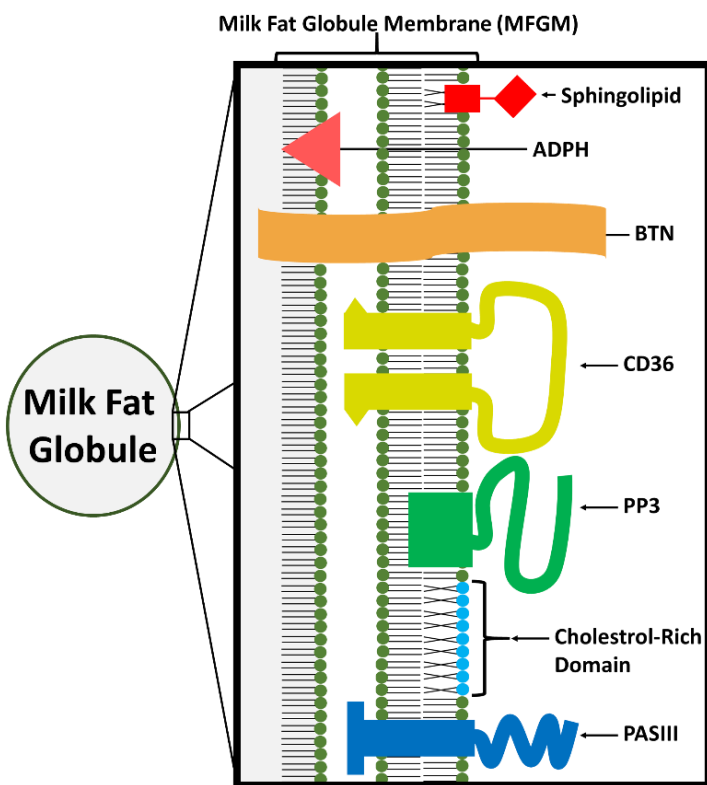
thickness of 10-50 nanometers.<sup>2</sup> The first layer is a monolayer of lipids, while the second layer is a bilayer of two lipid layers. Phospholipids and proteins make up 90% of the membrane's dry weight, with lipids and sphingolipids present in smaller amounts, functioning as signaling molecules.<sup>2</sup>

The MFGM contains various proteins, including adipophilin (ADPH), butyrophilin (BTN), cluster of differentiation (CD36), proteose peptone 3 (PP3), and mucin 15 (PASIII) (**Figure 3**).<sup>2</sup> Some of these components have shown antiviral activity and aid in milk production. The MFGM also features cholesterol-rich domains where cholesterol clusters. Notably, the MFGM composition is dynamic, with phospholipids, sphingolipids, lipids, and proteins constantly changing locations and transferring between membranes. This alteration can be seen during milk homogenization, which reshapes the NanoVehicles present in milk.

Homogenization of raw milk results in processed milk fat globules with diameters ranging from 200 to 2,000 nanometers. This process gives milk its rich, white color and smooth texture, while also inactivating bacteria and ensuring good quality and long-lasting milk. However, homogenization drastically changes the MFGM found in milk, reshaping the milk NanoVehicles. The membranes of milk fat globules are therefore dynamically complex, with unique structures composed of lipids and proteins.

#### 5. Other types of NanoVehicles

Milk and human breast milk contain NanoVehicles like emulsions of fat globules and casein micelles, which differ from other NanoVehicles like nanoemulsions, microemulsions, and micelles. These NanoVehicles have distinct physical properties and diameters, with milk NanoVehicles being larger and more complex.

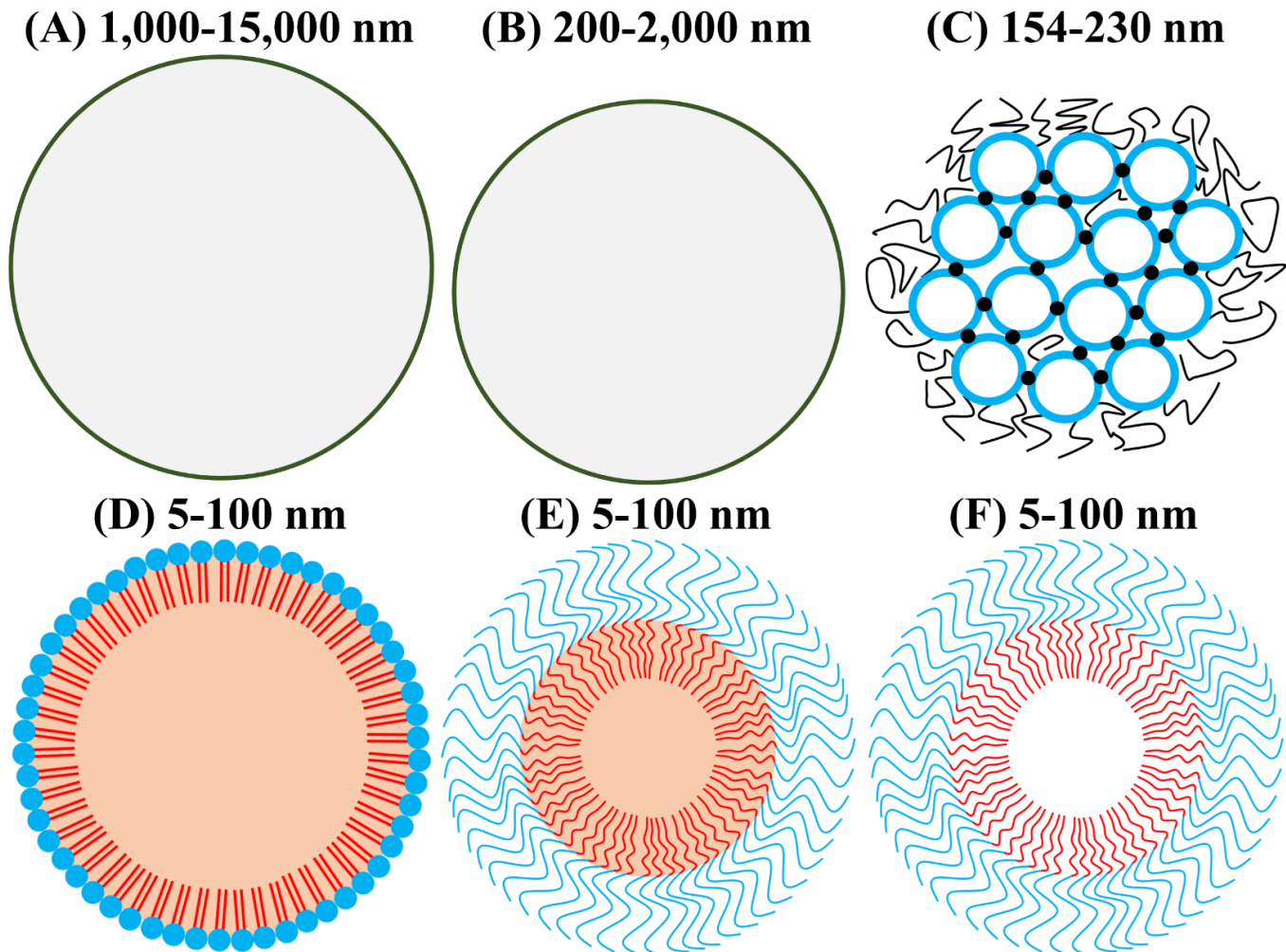


**Figure 3.** Schematic diagram representing the complex surface of the dominant milk NanoVehicle, otherwise known as milk fat globule membranes (MFGM). The diagram shows the various lipids and proteins that make up this type of milk NanoVehicle.

Nanoemulsions, microemulsions, and micelles are smaller and allow light to pass through their solutions, making them translucent or transparent. They are simpler than milk NanoVehicles and have diameters less than 100 nm.<sup>6</sup> Nanoemulsions are used in pharmaceuticals, particularly for cancer therapeutics and COVID-19 vaccinations, acting as

delivery vehicles for oil-loving ingredients.<sup>7-11</sup>

Microemulsions and micelles are similar to nanoemulsions but have distinct differences. They are bioengineered and simpler than milk NanoVehicles, with diameters similar to nanoemulsions. Microemulsions and micelles are



**Figure 4.** Schematic diagrams representing the sizes and structures of different NanoVehicles including (A) raw milk fat globules, (B) processed milk fat globules (C) casein micelles, (D) nanoemulsions, (E) microemulsions and (F) micelles. (A) The dominant milk NanoVehicle, otherwise known as raw milk fat globule, has diameters ranging from 1,000 to 15,000 nanometers and consist of a multi-layer membrane. (B) The processed milk fat globules have smaller diameters ranging from 200 to 2,000 nanometers. (C) Casein micelles contain calcium phosphate nanoclusters, and casein submicelles. (D) Nanoemulsions consist of an oil core that is surrounded with amphiphilic emulsifiers. These emulsifiers contain an oil-loving component that incorporates into the oil-core, and a water-loving component that interacts with water. (E) Microemulsions also consist of an oil core that is surrounded with amphiphilic emulsifiers. (F) Micelles are similar to microemulsions except that the oil core is missing. Nanoemulsions, microemulsions and micelles have diameters that range from 5 to 100 nanometers.

suitable for dietary supplements, as they can naturally form in the stomach and stomach acid. They require appropriate amphiphilic emulsifiers, which aid in delivery, absorption, and trafficking through the blood.

Dairy-free NanoVehicles like microemulsions and micelles are efficient delivery vehicles for oil-loving therapeutics or natural health ingredients in the blood. They have a longer water-loving component, which is essential for forming in the stomach and stomach acid and maximizing bioavailability and benefits.<sup>12,13</sup> These NanoVehicles have the potential to be highly impactful technologies for dietary supplements and will be discussed further in future white papers.

## 6. Conclusion

Milk from humans, cows, goats, and sheep has been a staple in the human diet for over 10,000 years. It consists of two types of NanoVehicles: milk fat globules and casein micelles. These NanoVehicles are complex structures that provide nutrition and are safe for consumption. Milk fat globules have diameters ranging from 1,000 to 15,000 nanometers, while casein micelles have diameters between 154 and 230 nanometers.

In contrast, nanoemulsions, microemulsions, and micelles are bioengineered NanoVehicles that are smaller and simpler in structure. Nanoemulsions require a high-energy process to produce and have diameters between 5 and 100 nanometers. They are currently used in cancer treatment and COVID-19 vaccinations, with significant benefits for patients.

The other dairy-free NanoVehicles, microemulsions and micelles, can be prepared in the stomach and stomach acid, making them a more natural option. They have the potential to be a highly impactful technology for dietary supplements, allowing for enhanced delivery of oil-loving natural health ingredients into the bloodstream. NanoPrime Labs has the technology to

incorporate these ingredients into dairy-free NanoVehicles, maximizing consumer wellness and health.

## 7. References

- (1) Atkins, P. *Liquid Materialities: A History of Milk, Science and the Law*; Routledge, 2016.
- (2) Argov, N.; Lemay, D. G.; German, J. B. Milk Fat Globule Structure & Function; Nanoscience Comes to Milk Production. *Trends Food Sci. Technol.* **2008**, *19* (12). <https://doi.org/10.1016/j.tifs.2008.07.006>.
- (3) Hristov, P.; Mitkov, I.; Sirakova, D.; Radoslavov, I. M. and G. Measurement of Casein Micelle Size in Raw Dairy Cattle Milk by Dynamic Light Scattering. *Milk Proteins - Struct. Biol. Prop. Health Asp.* **2016**. <https://doi.org/10.5772/62779>.
- (4) Hallén, E.; Wedholm, A.; Andrén, A.; Lundén, A. Effect of  $\beta$ -Casein,  $\kappa$ -Casein and  $\beta$ -Lactoglobulin Genotypes on Concentration of Milk Protein Variants. *J. Anim. Breed. Genet.* **2008**, *125* (2), 119–129. <https://doi.org/10.1111/j.1439-0388.2007.00706.x>.
- (5) Kunz, C.; Lönnerdal, B. Human-Milk Proteins: Analysis of Casein and Casein Subunits by Anion-Exchange Chromatography, Gel Electrophoresis, and Specific Staining Methods. *Am. J. Clin. Nutr.* **1990**, *51* (1), 37–46. <https://doi.org/10.1093/ajcn/51.1.37>.
- (6) Klang, V.; Valenta, C. Lecithin-Based Nanoemulsions. *J. Drug Deliv. Sci. Technol.* **2020**, *21* (1), 55–76. [https://doi.org/10.1016/S1773-2247\(11\)50006-1](https://doi.org/10.1016/S1773-2247(11)50006-1).
- (7) Tan, Q.; Liu, X.; Fu, X.; Li, Q.; Dou, J.; Zhai, G. Current Development in Nanoformulations of Docetaxel. *Expert Opin. Drug Deliv.* **2012**, *9* (8), 975–990. <https://doi.org/10.1517/17425247.2012.696606>.
- (8) National Institute of Allergy and Infectious Diseases (NIAID). *Phase I, Open-Label, Dose-Ranging Study of the Safety and*



- Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults*; Clinical trial registration NCT04283461; clinicaltrials.gov, 2020.  
<https://clinicaltrials.gov/ct2/show/NCT04283461> (accessed 2021-01-28).
- (9) Zhang, T.; Luo, J.; Fu, Y.; Li, H.; Ding, R.; Gong, T.; Zhang, Z. Novel Oral Administrated Paclitaxel Micelles with Enhanced Bioavailability and Antitumor Efficacy for Resistant Breast Cancer. *Colloids Surf. B Biointerfaces* **2017**, *150*, 89–97.  
<https://doi.org/10.1016/j.colsurfb.2016.11.024>.
- (10) Jokerst, J.; Lobovkina, T.; Zare, R.; Gambhir, S. Nanoparticle PEGylation for Imaging and Therapy. *Nanomedicine Lond* **2011**, *6* (4), 715–728. <https://doi.org/10.2217/nnm.11.19>.
- (11) Gabizon, A.; Shmeeda, H.; Barenholz, Y. Pharmacokinetics of Pegylated Liposomal Doxorubicin: Review of Animal and Human Studies. *Clin Pharmacokinet* **2003**, *42* (5), 419–436. <https://doi.org/10.2165/00003088-200342050-00002>.
- (12) Nieuweboer, A. J. M.; de Morrée, E. S.; de Graan, A.-J. M.; Sparreboom, A.; de Wit, R.; Mathijssen, R. H. J. Inter-Patient Variability in Docetaxel Pharmacokinetics: A Review. *Cancer Treat. Rev.* **2015**, *41* (7), 605–613.  
<https://doi.org/10.1016/j.ctrv.2015.04.012>.
- (13) Canada, H. *Pfizer-BioNTech COVID-19 vaccine: What you should know*. aem.  
<https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/pfizer-biontech.html#a1.1> (accessed 2021-02-01).

## 8. Disclaimer

The information in this white paper is for education and general information purposes only and has not been evaluated by the Food and Drug Administration (FDA). The information in this white paper is not implied or intended to be a substitute for professional medical advice, diagnosis, or treatment. The information and

products mentioned are not intended to mitigate, treat, diagnose, prevent or cure any medical condition. Please refer to the label on the dietary supplement bottle or website for interactions, cautions and safety data. You are strongly encouraged to consult with a qualified health care provider (pharmacist, registered dietitian, family physician, naturopath, etc.) if you have any health concerns or questions and interests about the use of dietary supplements. Any specific mention of a brand name is not a direct or indirect endorsement of that product.

The information in this white paper is the property of NanoPrime Labs LLC (NPL). All rights reserved 2024. None of the information presented in this white paper is permitted to be reproduced, copied or duplicated without the express written permission of NPL.

