FIRST MILKING BOVINE COLOSTRUM

Colostrum is a natural secretion produced by the mammary glands of all mammals that is intended for ingestion by the newborn during the first hours of life. In most mammals, such as humans, many of the biologically active substances in colostrum that are essential for development and survival of the fetus cross the placenta and reach the newborn prior to birth. However, bovines (cows) are very different and essentially none of the required biologically active substances cross the placenta. Instead, they remain in the mammary gland (udder) and must be conveyed to the calf by suckling during the early hours of its life. As such, complete bovine colostrum collected in the first hours after the calf is born is a unique, concentrated resource for a wide variety of highly beneficial biologically active substances.

The formation and delivery of colostrum in cows involves three processes that occur in association with the animal's mammary tissue. The first of these is **colostrogenesis**, which includes the events that influence the formation of colostrum. The second is **lactogenesis** or the process by which mammary tissue changes from the stage where it does not secrete fluid (non-lactating) to the stage where it does (lactating). The third process is called **galactopoesis** and it includes the steps through which the mammary gland shifts from the delivery of colostrum to the production of milk. Each of these processes is controlled by a specific set of hormones, but they are also influenced by several physical factors associated with the mammary gland. In the pregnant cow, development of mammary tissue with the ability to create substances and produce secretions is promoted mainly by growth hormone and associated insulin-like growth factors. The entire process is regulated by a series of hormones, the most important being progesterone, which attaches to special sites on the cells that line the interior of the mammary gland and prevents the cells from secreting any fluids into the gland until a few weeks before birth.

Colostrogenesis - the formation of colostrum.

The formation of colostrum in the pregnant cow starts about 3-4 weeks before birth of the calf when a very small amount of fluid is released into the developing mammary tissues. This fluid contains tiny amounts of growth hormone, insulin-like growth factors and other tissue transforming substances. The presence of these substances in the mammary gland stimulates the appearance of special active sites on the surface of the cells in the interior of the mammary gland. These sites will be used to transfer the substances necessary for the development and survival of the calf from the mother's bloodstream into the mammary gland. About two weeks before birth, more fluid enters the udder and some of the sites on the surface of the cells become fully activated. Immunoglobulin molecules (IgG) from the mother's blood attach to the active sites and are transported by specialized proteins through the cells into the fluid in the mammary gland. At the same time, specialized white blood cells from the mother attach to different active sites and are also transferred into the mammary gland. These cells immediately begin to release other immunoglobulin molecules (IgM and IgA) into the mammary fluid. Additional sites become activated during the 3-5 day period before birth and serve to transport the other biologically active substances from the mother's bloodstream into the mammary gland fluid.

About two days before birth, the hormonal balance and control of the mammary gland begins to change rapidly in the mother. The quantities of a hormone known as prolactin and, to a lesser extent, other hormones increase sharply in the mother's bloodstream, removing some of the inhibitory effects of progesterone. This starts the production of large volumes of fluid that fills the mammary gland and also turns on the ability of cells in the mammary gland to make certain substances, like lactose (milk sugar). When birth occurs and the placenta is eliminated, the amount of progesterone in the blood of the mother drops dramatically and its control over the secretions in the mammary gland is completely removed. At the same time, a unique protein develops inside the cells lining the mammary gland. This protein completely blocks the process by which biologically active substances were transferred from the mother's bloodstream into the mammary gland. Therefore, at this point, the composition of colostrum in the mammary gland represents true and complete colostrum that is maximally enriched with the biologically active substances required to support the development and well-being of the calf. In addition to being a thick, golden-colored liquid, this material has the following characteristics:

- a high protein concentration, a large portion of which is IgG;
- the highest concentration of growth promoting substances, other hormones and additional biologically active substances;
- rich in milk fat; and
- low in lactose.

Lactogenesis - getting ready to secrete colostrum.

The process by which the cow begins to prepare to secrete the fluids developed in its mammary gland, or lactogenesis, starts before colostrogenesis finishes. When the level of progesterone in the mother's bloodstream begins to fall a few days before birth, significant volumes of fluid begin to enter the mammary gland, although the volumes that enter are not as great as will occur after birth. At this point in time, it is physically possible to remove some colostrum from the mammary gland, however, the colostrum usually is not fully formed and the removal has been shown to diminish the quantity and quality of fluid collected after birth. Fully functional lactation in the cow begins within moments after birth when the placenta is eliminated and all inhibition of secretions by progesterone is removed.

Galactopoeisis - the production of milk.

The potential to produce milk within the mammary gland also occurs almost simultaneously with elimination of the placenta and removal of the controlling effects of progesterone. After birth, one of the most influential factors on the composition of what will be secreted from the mammary gland is physical removal of the fluid within the gland. During the hours after birth, removal of even a small amount of fluid from the gland results in the production of very large amounts of fluid by cells in the gland itself. Since the transfer of biologically active substances from the mother's bloodstream was blocked at birth, all of the substances found in the added fluid will have been made by cells in the gland itself and the composition of the remaining fluid will change. This secondary fluid that is produced wholly by the mammary gland after birth, but may contain remnants of the original colostrum, is called "transitional milk". Thus, the larger the quantity of original complete colostrum removed at the first milking after birth, the more adulterated the remaining colostrum becomes with transitional milk.

Factors that affect colostrum composition.

Another important characteristic that influences the composition of colostrum is the fact that, if the colostrum is not removed from the mammary gland within 6 hours after birth, the mother's system will begin to reabsorb many of the biologically active substances, including the hormones and immunoglobulins, back into her bloodstream from the mammary gland. Therefore, the composition of the secretions from the mammary gland change rapidly during the hours and days after birth so that there is a continuous transition from complete colostrum to whole milk. These changes are evident from the values shown in the following chart taken from Fundamentals in Dairy Chemistry, a reference book for the dairy industry published in 1978.

COMPOSITION OF
BOVINE COLOSTRUM & TRANSITIONAL MILK

Hours After Calving	% Total Protein	% Fat	% Lactose	% Total Solids
0	17.57	5.10	2.19	26.99
6	10.00	6.85	2.71	20.46
12	6.05	3.80	3.71	14.53
24	4.52	3.40	3.98	12.77
48	3.74	2.80	3.97	11.46
72	3.86	3.10	4.37	11.86
96	3.76	2.80	4.72	11.85

As can be seen from this chart, complete colostrum is made up of about 27% solid material and 73% water at the time of birth. About 65% of the solids are proteins and approximately 40% of these proteins are immunoglobulins, mostly IgG. If no fluid is physically removed from the udder within 6 hours after birth, the amount of solids drops by about 25%; the protein content is reduced by more than 40% and the total proteins now are only 50% of the total solids. Six hours later, at 12 hours after birth, the total solids are only about 55% of what they were at the time of birth and only 40% of the solids are proteins. This change is even more dramatic by 24 hours after birth and continues as the mother reabsorbs unutilized biologically active substances from her mammary gland. In addition to the loss of material due to reabsorption, the fluid in the mammary gland reflects other changes that are ongoing after birth, including the production of lactose by cells that line the mammary gland and the slowing of fat production.

The average amount of colostrum that can be collected from a mature Holstein dairy cow in the first milking taken within the first 6-8 hours after birth is approximately 10 liters (9.5 quarts). Since the inner surface of the udder has folds and wrinkles in it, not more than 80% of the fluid in the udder can be removed in a single milking. The remaining 20% is trapped in the folds and wrinkles and is diluted with the transitional milk that is generated by the cells inside the mammary gland to replace the fluid that was removed. Therefore, the second milking after birth, even if it is taken within the first 6 hours, only contains 20% of the original complete colostrum that was present in the mammary gland at birth. The same 80/20 rule applies every time the udder is emptied and, thus, each succeeding milking proportionately dilutes the residual original complete colostrum left in the mammary gland until the resulting fluid has the composition of whole milk.

When the facts are put into perspective, it is easy to understand how important it is to collect the maximum amount of colostrum in one milking as soon after birth as possible and definitely not more than 6 hours after the calf is born. This is the material that contains the maximum amount of biologically active substances and is known as complete first milking bovine colostrum.

Colostrum and the calf.

Everyone who uses colostrum worries that the dairy farmer is going to collect as much colostrum as he can and then sell it without giving any to the calf. First, we have to understand that the calf in question is valuable to the dairy farmer as a replacement or expansion animal in his herd, so he is going to do everything that he can to help that calf survive and develop into a healthy, producing animal. In fact, modern dairy farmers in the United States recognize that allowing the calf to suckle its mother usually results in the calf receiving less colostrum than it should. Numerous scientific studies have shown that a calf must receive about two quarts of colostrum within 6 hours after it is born to minimize its risk of disease and support its development as a healthy and productive animal. If allowed to suckle, the calf will usually do so for about 10-15 minutes after birth and then will sleep for several hours; arise, suckle for 10-15 minutes and then sleep again for several hours; repeating this process for a few days until it gains strength. The first suckling alone removes only a small amount of colostrum, but causes the generation of a substantial amount of transitional milk, significantly diluting the residual colostrum. This dilution effect is magnified during each successive suckling by the calf, limiting the amount of beneficial biologically active substances it can receive.

Most dairy farms in the United States maintain a separate maternity ward and nursery where they monitor pregnant cows 24 hours a day during the week just prior to delivery. When the calf is born, it is immediately removed from its mother and not allowed to suckle. The colostrum is collected in a single unit within a few hours after birth and the calf is hand-fed two quarts in a nursing bottle before it is 6 hours old. This approach not only assures that the calf got enough colostrum when it needed to in order to maximize the benefits, but it also keeps the calf from making contact with the soiled udder and fecal material from its mother and other cows, which are recognized resources for the transfer of infectious microorganisms.

There is a considerable body of scientific evidence that a calf that fails to receive an adequate quantity of high quality complete colostrum shortly after birth will have a reduced capability to protect itself against pathogenic microorganisms in its environment. In addition, if the animal survives, it will have a higher incidence of illness and it will develop less body mass than normal. The impact of inadequate colostrum intake during the first hours of life on the survival and health of calves was studied in more than 2,200 animals over a five year period by the United Kingdom National Agricultural Center Calf Unit. As shown in the table, they found that calves that received only a small amount of colostrum were six times more likely to die than those that received the required two quarts. If the animals that received a small amount of colostrum survived, they were ill almost three times as often as the calves that got enough colostrum. Getting enough high quality colostrum is essential to the health and well-being of the calf and failure to do so will follow the animal for the rest of its life. Dairy farmers say "how a calf starts determines how the cow finishes".

EFFECT OF COLOSTRUM INTAKE ON CALF HEALTH

Colostrum Intake	% Died	% Ill
Little	7.9	42.2
Some	3.0	24.2
Enough	1.3	15.4

The rapidly changing composition of colostrum in the mammary gland of the mother fits together very well with events that happen in the body of the newborn calf. During the first six hours of life, the calf's stomach lining does not make any acid and there are very few, if any, enzymes present that can break down ingested proteins. Complete first milking colostrum also contains substances that inhibit the action of some enzymes. Therefore, these conditions work in favor of having the biologically active substances in complete colostrum pass through the calf's stomach into the upper portion of the small intestine without being broken down. During the first 6-8 hours of life, this area of the small intestine has specialized sites where the biologically active substances can be absorbed and transported directly into the calf's bloodstream. After this period, the stomach begins to acidify, enzymes appear and the specialized absorption area in the small intestine changes dramatically so that most of the biologically active substances in colostrum are no longer absorbed. This process is aided by the fact that calves are born with a well-developed system of lymphoid tissue under their tongue and at the back of their throat that persists throughout their entire life. Many biologically active substances are absorbed through these tissues when the calf suckles its mother or a nursing bottle. In adults, this is a major route for absorption of beneficial substances from food, without subjecting them to degradation in the digestive tract, as the animal "chews its cud".

Comparison of bovine and human colostrums.

Colostrum has evolved in nature as a nutritional supplement that is fed to the newborn by its mother during a short period after birth. Its natural evolution can be shown to follow a path that meets the immediate demands of the newborn and, since most species of mammals develop at different rates and have different nutritional requirements, the colostrum and follow-on milk of each species has a different composition. Some colostrums are very similar and some are extremely different. The composition of bovine colostrum is quite different from the colostrum produced by humans.

The most substantial difference is found in the immunoglobulin (antibodies) content of these colostrums. In humans, the IgG immunoglobulins are conveyed from the mother's bloodstream through the placenta while the fetus is still in the mother's uterus and are not found in the colostrum. This provides some degree of temporary passive immunity to the newborn against possible infectious agents after birth. In contrast, none of the immunoglobulins in the pregnant cow's bloodstream are transferred across the placenta and, thus, the calf is essentially defenseless when it is born unless it gets colostrum. The major immunoglobulin found in bovine colostrum is, therefore, IgG, but, although there is only a small amount of immunoglobulins in human colostrum, the major one is IgA. The immunoglobulin (IgA) in human colostrum and milk is unique in that it has a special protein fragment attached to it that is believed to protect it from the effects of stomach acid and digestive enzymes.

It must also be recognized that since the immunoglobulins are transferred across the placenta in humans, many of the essential growth factors are also transferred. Therefore, human colostrum and the milk that follows become supplementary resources for these biologically active substances and the newborn can survive and develop without receiving them by suckling. In contrast, none of these factors are transferred across the placenta in the pregnant cow and, as discussed earlier, calves that do not receive enough colostrum suffer serious deficiencies in the development of their immune system and their body mass.

Bovine and human colostrum also differ in other ways that reflect the different needs of the respective newborns. For example, human colostrum and milk contain the highest amount of lactose (milk sugar) of any species. The lactose provides about 40% of all of the calories available to the suckling infant. The high lactose content is believed to serve two purposes: (1) the infant brain is very large, much larger than any other species, and requires a lot of glucose to develop rapidly; lactose is easily broken down into glucose and galactose before it is absorbed by the intestines; and (2) for physical chemical reasons, the high lactose content causes the secretion of a large amount of water into the mammary gland, assuring that the infant's needs to support fluid loss through sweating and urine formation are met.

Bovine colostrum and milk contain substantially more casein than is found in human colostrum or milk. Casein is a complex protein that is acted upon by enzymes in the stomach to form a curd that has the consistency of cottage cheese. In the calf, this curd is much harder than the curd that forms in babies that are nursed. The curd allows time for additional enzymes to break the protein down into small peptides and amino acids. These breakdown products are absorbed into the body and serve as the building blocks for new proteins to build muscle. The extra casein in bovine colostrum and milk reflects the need for a ready source for more muscle-building capacity since the body mass of a calf develops much more rapidly than that of a newborn baby.

Colostrum is an amazing material that, like many other things in nature, reflects the evolutionary development of a unique composition that will serve the needs of the offspring for which it is intended. **The most unique of the colostrums from mammalian species occurs in bovine species where everything required for the development of a healthy, productive offspring is provided in the colostrum. As such, it represents a specialized resource that offers the broadest possible spectrum of biologically active substances that can promote the development of a sound body mass and support the activation and maintenance of a fully functional immune system capable of efficiently and effectively combating potential insults from microorganisms and other deleterious sources. Bovine colostrum is also compatible with almost any species and can readily convey its full benefits to humans by routine dietary supplementation**.

THE COMPOSITION OF BOVINE COLOSTRUM

The previous section provides an insight into how bovine colostrum is formed and describes what complete first milking colostrum really is. This section discusses in some detail what it is composed of and the nature of the major biologically active components.

The basic composition of colostrum.

As indicated in the earlier section, complete first milking bovine colostrum is a thick, golden-colored fluid that contains a lot of proteins, many of which are biologically active; is rich in milk fat; and is low in lactose (milk sugar). The best way to understand what colostrum should be composed of is to look at how the relationship of these three major components changes with time after birth of the calf. In this case, the basic values shown for liquid colostrum in the last section have been converted to what would be found in the same colostrum if it was dried in powder form, the way most people use colostrum as a dietary supplement.

COMPOSITION OF
DRIED BOVINE COLSTRUM & TRANSITIONAL MILK

Hours After Calving	% Total Protein	% Fat	% Lactose
0	65.10	18.90	8.11
6	48.90	33.48	13.25
12	41.64	26.15	25.53
24	35.40	26.62	31.17
48	32.64	24.43	34.64
72	32.55	26.14	36.85
96	31.73	29.60	39.83

It is really obvious how fast the relationship of these components changes after birth of the calf. This changing relationship is extremely important in establishing that the best colostrum is used and in assuring that it contains the maximum amount of biologically active substances.

Protein.

Most of the biologically active substances in complete bovine colostrum that can convey significant health benefits are proteins. As you can see, **the protein composition of colostrum changes rapidly after birth. Since almost all of the beneficial proteins are conveyed from the mother's bloodstream into the colostrum before birth and the mother then begins to reabsorb them after birth, it is important to use colostrum that has been collected during a time period that will minimize the effect of the reabsorption process**. The first section described the 80/20 rule and the diluting effects of transitional milk when colostrum is removed, so it is also very important to assure that only complete first milking colostrum was used. The whole concept for defining the value of first milking colostrum taken within 6 hours after birth has been established by a number of scientific studies. Of real significance is the finding that by 24 hours after birth most of the proteins in the udder fluid can be accounted for by two individual proteins that are primarily only of nutritional value. They are casein, which was discussed in the fist section, and albumin, which is similar to the albumin found in egg whites. Since we cannot collect colostrum at the time of or within minutes after birth, good quality complete first milking colostrum will contain 45-60% protein, of which about 40% will be immunoglobulins.

Colostral Fat.

The milk fat in complete first milking colostrum is one the most under-rated and misunderstood components by many companies that promote bovine colostrum for human consumption. There are all kinds of stories, none of which are ever substantiated with any scientific evidence. One of these says that the fat in colostrum doesn't serve any purpose and/or that having it there leads to faster deterioration of the product. Nothing could be further from the truth. In fact, one of the companies that removes the fat from what they call "colostrum" adds a component of the fat back to their dried products. They claim that this makes their "colostrum" more digestible, which was one of the functions of the fat in complete colostrum in the first place. Remember from the last section how casein is broken down in the stomach to small peptides and amino acids so that they can be absorbed and used to build new muscle protein by forming a cottage cheese-like curd in the stomach. This occurs enzymatically in the newborn and the adult. The basis for the curd that forms is the fat in the colostrum. So without it, in addition to losing some significant biologically active substances that are associated with the fat, most of the nutritional value of the casein is also lost. That is part of the reason why the fat content of colostrum increases with time after birth as the amount of casein increases in the secreted fluid. **Mother Nature doesn't waste much and has organized the components of colostrum and their changing pattern in an efficient way to maximize the benefits to the offspring that is going to receive it.**

High quality first milking bovine colostrum will contain 20-30% milk fat. The milk fat in colostrum is also a very important means to deliver some of its beneficial biologically active substances. Dissolved in or associated with the fat in colostrum are the following substances.

- Vitamins A, D, E and K
- Steroid hormones
- Corticosteroids
- Some growth factors
- Insulin

Lactose (milk sugar).

As can be seen from the chart above, in high quality complete first milking colostrum 10-15% of all of the solid material in the fluid will be lactose. We discussed earlier how important the lactose is to the calf as an immediate energy source when it is broken down to glucose and galactose by an enzyme (lactase) in the saliva and the stomach. Therefore, it makes good sense that the amount of lactose in transitional milk and mature milk increases as the body mass of the calf develops rapidly during the early days of its life.

Since most people have the same enzyme (lactase) in their saliva and their digestive system, the lactose in the colostrum that they use as a dietary supplement can provide the same ready source of energy. However, there are individuals who have problems digesting lactose because their body produces too little or none of the lactase enzyme. They are said to be "lactose intolerant". This problem occurs more frequently in individuals of Asian and Latin American descent, but is found in people of all ethnic backgrounds. As shown in the chart, the amount of lactose in first milking colostrum collected within 6 hours after birth is about one-half of what it is at 12 hours after birth and one-third of what it becomes by 24 hours. Therefore, a high quality complete first milking colostrum collected within 6 hours after birth can be used as a dietary supplement by more people without potentially having them suffer the discomforts associated with lactose intolerance.

Other compositional changes.

The following comparative facts about colostrum and milk further stress the need to use a complete first milking colostrum in order to maximize the benefits that it can provide.

- Colostrum contains 10 times more vitamin A than milk.
- Colostrum contains 3 times more vitamin D than milk.
- Colostrum contains at least 10 times more iron than milk.
- Colostrum contains more calcium, phosphorous and magnesium than milk.

The biologically active components.

The biologically active components in complete first milking colostrum can be divided into categories based upon the health aspect where they exert their greatest influence. As we go through the discussion of what these substances do, it can be seen that, in some cases, the functions of these components can be clearly separated into such categories, while, in many cases, the dividing line is clouded. The major categories are the Immune Factors, the Growth Factors and the Metabolic Factors. In this section, we intend to make you familiar with the substances in these categories. However, before we begin this discussion, it is very important to recognize that most of the very broad claims about what these substances do that are made by many other suppliers of colostrum for human consumption are based upon very specialized studies in experimental animals, like mice or rats, and represent **the company's interpretation of the results** and **not necessarily that of the original scientific investigator.**

The Immune Factors.

To comprehend what the Immune Factors are in high quality first milking colostrum and what they do, it is important to recognize that some of these components have one or more effects on the overall regulation and functioning of the immune system (immuno-regulating substances), while others are very restricted in what they can do and their benefits are usually very localized in the body, ordinarily exerting their effects primarily in the gut (gut protective substances).

Immuno-regulating substances.

- **Thymosin (alpha & beta chains).** A hormone composed of two protein-based chains that are separately present in bovine colostrum. The chains act on the thymus gland independently or in concert with each other to stimulate activation, development and maintenance of the immune system.

- **Proline-rich peptide (PRP).** A hormone-like small protein that acts upon the thymus and other organs associated with the immune system to keep it from over-reacting to an insult.

- **Cytokines.** Small proteins produced by various cells in the body that induce the generation of specialized types of white blood cells, signal them to come to the site of an insult and help in their passage through tissues.

- **Lymphokines.** Proteins of varying sizes that are produced by different types of white blood cells that tell related cells to transform themselves into more functional cell types that can release substances capable of destroying an invading microorganism.

Gut protective substances.

- **Immunoglobulins (IgG, IgM, IgA).** Complex proteins, better known as antibodies, that make up a significant portion of the proteins found in complete first milking colostrum. These antibodies were produced by the mother's immune system in response to her exposure to many different microorganisms during her lifetime and then transferred into the colostrum prior to birth of the calf. There is no evidence that any of these antibodies are found intact in the blood of individuals who ingest colostrum by mouth. However, many of these antibodies are reactive against bacteria, viruses and fungi that infect the gastrointestinal tract of humans and there is scientific evidence that some of them can survive passage through the digestive system.

- **Transfer factors.** Small proteins produced in response to the body's exposure to certain types of microorganisms, particularly those that reside in deep tissues for a long period of time, like the bacterium that causes tuberculosis. They are specific for a particular microorganism and are carried inside of certain types of specialized white blood cells. Transfer factors have limited effectiveness alone in defending the body against infection by such microorganisms, but, rather, act in concert with various white blood cells and other factors in an attempt to keep the microorganisms under control.

- **Lactoferrin.** A mineral-binding carrier protein that attaches to available iron. Certain aerobic (grow in the presence of oxygen) bacteria, like *E. coli*, require iron to reproduce and, therefore, lactoferrin is an effective substance, when operating in the presence of a specific antibody, to impede the growth of some microorganisms in the gut. A broad number of additional claims have been made by some providers of colostrum for human consumption regarding the application of lactoferrin as an immuno-regulating substance with antiviral, antibacterial and anti-tumor properties. To date, none of these claims have been adequately substantiated through properly controlled studies.

- **Transferrin.** Another mineral-binding carrier protein that attaches to available iron and can act independently or in concert with lactoferrin to impede the growth of certain aerobic bacteria, particularly in the gut.

- **Lysozyme.** A very powerful enzyme that is capable of attaching itself to the cell wall of certain pathogenic bacteria and degrading select components, leaving holes in the wall of the bacteria.

- **Lactoperoxidase.** A mildly effective enzyme that can also attach to the wall of certain bacteria, degrade selected proteins and interfere with the ability of the bacteria to replicate themselves.

- **Xanthine Oxidase.** Another mildly effective enzyme that can also attach to the wall of certain bacteria, degrade different proteins than those affected by lactoperoxidase and, therefore, also interfere with the ability of the bacteria to replicate themselves.

- **White blood cells (leukocytes).** Primarily, three types of functional white blood cells are present in colostrum, including neutrophils, macrophages and polymorphonuclear cells. Each has the ability to phagocytize (engulf) microorganisms and other foreign bodies and apply substances carried internally to the destruction of the microorganisms. Their functions are dramatically enhanced when antibodies first attach to the microorganisms.

- **Oligosaccharides and glycoconjugates.** Complex carbohydrates (sugars) that can adhere to specific sites on the inner surface of the gastrointestinal tract and prevent the attachment of microorganisms.

The Growth Factors.

- **Growth hormone.** Very small quantities of growth hormone are found in complete first milking colostrum, but that is all that is required since this hormone is extremely potent. It has a direct effect on almost every cell type and significantly influences the proliferation of new cells, particularly their rate of generation. Scientific studies have shown that continued ingestion of small amounts of growth hormone are beneficial in limiting the ongoing deterioration of cells associated with the aging process.

- **Insulin-like growth factors (IGFs).** Insulin-like growth factor-1 (IGF-1) and its closely related counterpart insulin-like growth factor-2 (IGF-2) are potent hormones that are found in association with almost all cells in the body. They are part of a group of more than 90 different proteins, called the "IGF Binding Protein (IGFBP) Superfamily", that is responsible for the processes by which cells grow and reproduce. These substances are also responsible for maintenance of the metabolic pathways in the body by which cells convert glucose to glycogen, a primary energy resource, and use amino acids to create proteins. The key event that triggers the functions of the various proteins in the IGFBP Superfamily is the attachment of IGF-1 to a specific site on the surface of a cell. Many of the growth factors found in colostrum and previously defined by their functions are now considered part of the IGFBP Superfamily. This includes the following substances, among others.

    - **Transforming growth factors A & B.** Induces the transformation of cells from an immature form to a mature, functional status.

    - **Epithelial growth factor.** Involved in the generation and maintenance of cells in the epithelial (outer) layers of the skin.

    - **Fibroblast growth factor.** Associated with the regeneration of various types of tissue, including skin and other organs.

    - **Platelet-derived growth factor.** Responsible for the generation of cells and functions associated with blood clotting.

The Metabolic Factors.

- **Leptin.** A small hormone-like protein that can suppress appetite and lead to body weight reduction. Mature fat cells (adipocytes) release leptin in the presence of insulin, which is also found in colostrum. Insulin-producing pancreatic beta-cells have binding sites for leptin and it is believed that the size of fat cells may be a major factor in determining the amount of leptin released. Therefore, leptin deficiency may be associated with obesity, particularly in diabetic individuals.

- **Insulin.** A hormone required for the effective utilization of glucose (blood sugar) in the body. Insulin binds to specific sites on cells, facilitating their interaction with IGF-1 and, thus, initiating the conversion of glucose to glycogen, a high energy source carbohydrate.

- **Vitamin-binding proteins.** Smaller proteins that act as carriers to deliver B-complex vitamins to the body. Carrier proteins and the associated vitamins folate (B6), B12 and orotic acid are found in colostrum.

- **Fat-associated vitamins.** Significant quantities of vitamins A, D, E and K are dissolved in or associated with the fat in colostrum.

- **Mineral-binding proteins.** The iron-binding proteins, lactoferrin and transferrin, have already been discussed above. In addition to interfering with the replication of certain microorganisms, they also serve to capture iron from the ingested food and present it in a form that can readily be absorbed by the body. Lactoferrin can also bind copper and deliver it in a form suitable for absorption by the body. In addition, there are two carrier proteins in colostrum that assist in the absorption of calcium. They are casein, which is also an abundant source of amino acids to build new protein molecules, and alpha-lactalbumin, which is present in colostrum very soon after birth.

- **Cyclic adenosine monophosphate (cAMP).** A phosphorylated nucleotide in a very specialized form that transfers the chemical energy necessary to drive metabolic reactions to form new protein, carbohydrate and fat molecules.

  - **Enzyme inhibitors.** These have been called "permeability factors" by other manufacturers, but are actually small proteins that slow down or inhibit the breakdown of proteins by certain enzymes. They provide limited protection to the immune, growth and metabolic factors as they pass through the digestive tract.

There are many other substances present in colostrum, but very few of them are of any significance since they are present only in very minute quantities and they provide little on no benefit to humans who ingest colostrum routinely as a dietary supplement. However, there are two substances, in addition, to those described above that do provide significant benefits. They are the hormone **melatonin**, which has a direct effect on the establishment of biological rhythms and proper sleep patterns; and **relaxin**, a hormone known to directly affect contracted muscles.

CHARACTERIZATION OF COLOSTRUM PRODUCTS

IMMUNO-DYNAMICS

To assure that bovine colostrum contains the maximum amount of the available biologically active substances, it must be collected only at the first milking within six hours after the birth of the calf. In addition, the final product must be of the same relative composition as the original colostrum and not contain any additives or supplements in order to assure the intactness and functionality of the biologically active components. Only colostrum products that meet these criteria are capable of delivering the maximum benefits available through routine use.

The following sections examine the characteristics of the colostrum powder produced by Immuno-Dynamics and some of its competitors in terms of their chemical composition and the content of specific components. The values shown in the tables and graphs were derived from assays conducted independently and without bias by a highly regarded dairy testing laboratory and the diagnostic laboratories of a major college of veterinary medicine.

Basic Chemical Composition

As discussed earlier, the best way to understand what colostrum should be composed of is to look at how the relationship of three major components, protein, fat and lactose, changes with time after birth of the calf. In the table below, the basic values shown in earlier tables have been converted to the true unit of mass that would be found in each gram of colostrum powder.

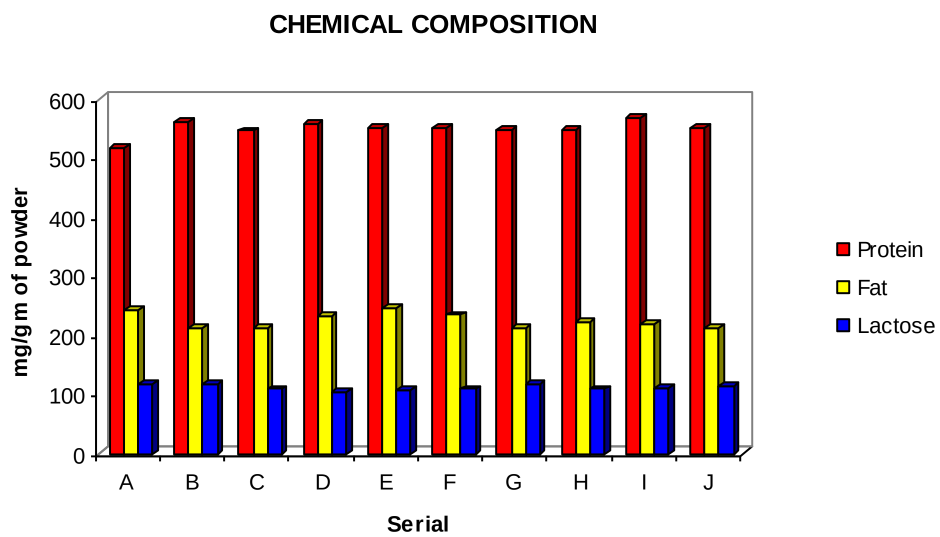
Composition of Bovine Colostrum
(mg/gm of total solids)

Hours After Birth	Total Protein	Fat	Lactose
0	651.0	189.0	81.1
6	489.0	334.8	132.5
12	416.4	261.5	255.3
24	354.0	266.2	311.7

The comparative chemical compositions of ten (10) serials of colostrum powder manufactured from large pools by Immuno-Dynamics are detailed in the following table. The same data is also graphically displayed. Comparison of these data with the values given in the table above clearly indicates that the serials are all composed of colostrum collected within six (6) hours after birth of the calf in a single milking. In addition, the consistency of the values, reflecting the lot-to-lot reproducibility of the product, is immediately apparent.

CHEMICAL COMPOSITION
(mg/gm of powder)

Serial No.	Total Protein	Fat	Lactose
A	516.8	243.8	117
B	559.7	211.7	117
C	545.4	211.0	109
D	557.7	233.5	105
E	549.3	246.0	106
F	549.0	233.8	109
G	547.7	211.8	118
H	546.6	221.0	109
I	568.0	220.1	110
J	556.7	212.1	113
Mean	549.7	224.5	111.3
S.D.	13.371	13.773	4.692
95% Interval	26.742	27.546	9.384
Range	522.96 - 576.44	196.95 - 252.05	101.92 - 120.68



Biologically Active Components

A series of eight (8) of the biologically active components of bovine colostrum were selected as the marker components based upon a) the availability of an immunoassay for the determination of concentration; b) the ability of the assay or an adaptation thereof to perform reliably with colostrum; an c) the importance of the role of the component in the biological effects observed with colostrum.

- **Insulin–Like Growth Factor–1 (IGF-1)**

Insulin-like growth factor-1 (IGF-1) and its closely related counterpart insulin-like growth factor-2 (IGF-2) are potent hormones that are found in association with almost every cell in the body. IGF-1 is the most potent and best described of this pair. These molecules are present in all mammals and, in every case, have a very similar chemical structure regardless of the species. IGF-1 is absolutely necessary for normal cell growth and for the development of the fetus in the uterus. Both IGF-1 and growth hormone are also required for normal development outside of the uterus and that is why they are both present in colostrum. The chemical structure of the IGFs is very similar to insulin and that is where their name comes from.

Scientific knowledge about the IGFs, what they do and how they act on cells in the body has developed very quickly during the past few years. It is now known that there are specific sites, called receptors, on almost all cells in the body capable of interacting with IGF-1. These sites have a structure that fits perfectly with part of the IGF molecule and this interaction triggers a series of chemical events within the cell. There are also 6 different proteins present inside the cell and on the surface of the cell that react to the attachment of IGF-1 to its receptor. These are called insulin-like growth factor binding proteins (IGFBPs) and they control the actions of IGF-1 on the cell. In addition, inside the cell there are at least 87 other related proteins either capable of binding to IGF-1, altering its actions, or influencing the effects of the IGFBPs. These are called insulin-like growth factor binding protein-related proteins (IGFBP-rPs). The entire collection of these proteins is referred to as the Insulin-like Growth Factor Binding Protein (IGFBP) Superfamily. The key event that triggers the effects of any of these proteins appears to be the interaction of IGF-1 with its specific cell-surface receptor, an event that some of these proteins regulate.

The multitude of available IGF-1binding proteins and related proteins available in the cell is indicative of the many potential effects that the binding of IGF-1 to its specific cell-surface receptor can have on cells. To keep these many effects under control, some of the binding proteins act as checks and balances, allowing the secondary chemical switches in a cell to be turned on and then turning them off when it is appropriate. Therefore, IGF-1 is like the captain of a ship. When it binds to its specific receptor, the ship can move forward, but there are all kinds of systems in place to keep it moving at the right speed and in the right direction.

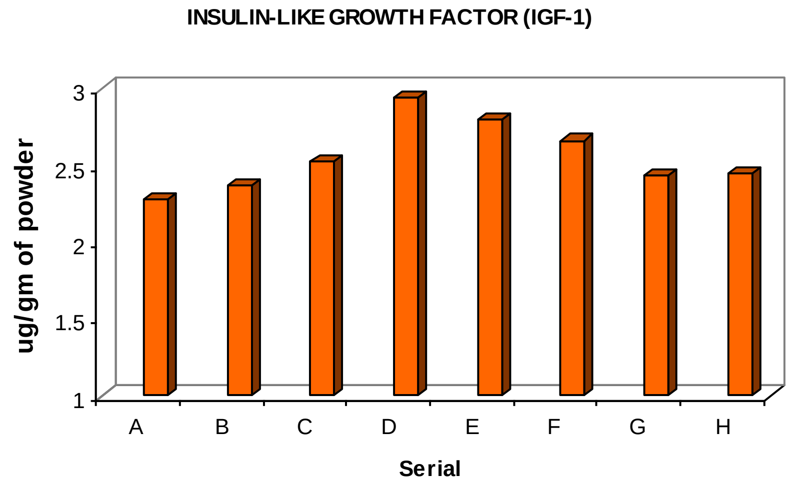
The main triggered events include activation of the process by which the cell grows and reproduces itself and maintenance of the metabolic pathways by which the cell converts glucose into glycogen and uses amino acids to create proteins. The actual pathway by which the cell uses glucose and converts it to glycogen is first switched on by the binding of insulin to its specific cell surface receptors. As indicated earlier, glycogen is stored in the liver and muscles and is the reserve source of readily available energy when the muscles are exercised.

The IGFBP Superfamily also has a direct role in how the cell uses amino acids to build proteins. As the body of any mammal ages, its ability to create an adequate supply of IGF-1 is diminished. Thus, eating a well-balanced diet and maintaining a constant supply of IGF-1 in the body, keeps the ship moving at the right speed and in the right direction. And when the body is exercised, this becomes even more critical since there is an increased demand for glycogen to provide energy to the muscles and the preference is to build more muscle protein. Even more importantly, as the cells in the body age, they do not reproduce themselves as well and, since IGF-1 is a primary factor, along with growth hormone, in the ability of cells to grow and reproduce, it is highly desirable to have an appropriate level of IGF-1 in the circulation through dietary supplementation to limit the ever increasing rate of cell death.

Biologically Active Components

IGF-1, Leptin, Insulin
(mass/gm of powder)

Serial	IGF-1 (ug/gm)	Leptin (ng/gm)	Insulin (mIU/gm)
A	2.277	91.82	1.294
B	2.366	138.00	1.508
C	2.526	114.18	1.728
D	2.940	133.18	1.417
E	2.801	145.82	1.517
F	2.665	110.27	1.195
G	2.440	120.64	1.264
H	2.453	93.91	1.076
Mean	2.723	118.45	1.375
S.D.	0.226	19.819	0.209
95% Int	0.452	39.638	0.418
Range	2.271 - 3.175	78.82 - 158.09	0.957 - 1.793



A high quality bovine colostrum must contain at least 2.25 micrograms of insulin-like growth factor-1 per gram of powder to provide maximum benefits to the end-user. The colostrum powder produced by Immuno-Dynamics always contains more than the minimum level of this important constituent. In addition, these assays confirmed the lot-to-lot consistency of the concentration of this component.

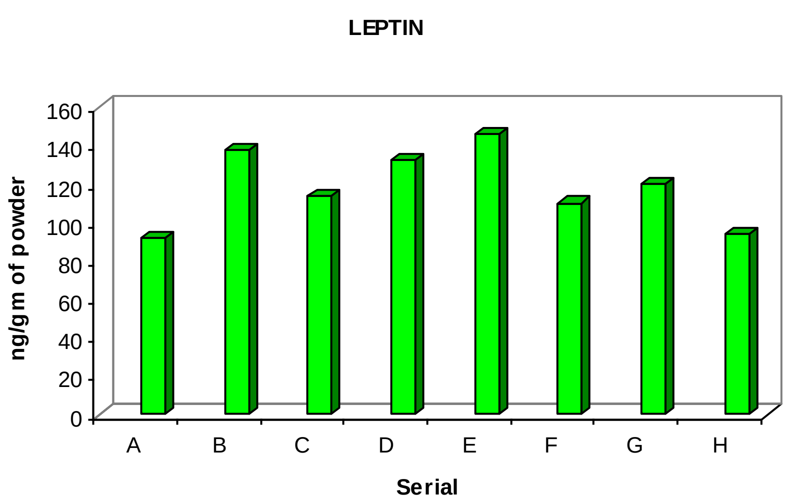
- **Leptin**

Leptin is a small, hormone-like protein that is produced primarily by adipocytes (fat cells) and in smaller amounts in some other peripheral organs. Small adipocytes produce more leptin than large adipocytes, which are predominant in obese individuals. Leptin operates in the presence of insulin by linking to cell surface receptors, which are binding sites specific for leptin on the outside of the cell. This interaction results in transmission of a chemical signal to the hypothalamus, causing a suppression of appetite with a simultaneous stimulation of metabolism. Leptin and leptin receptors are also present in the cells of the lining of the human small intestine where the effects on appetite suppression are local rather than systemic. Ingestion of small amounts of alcohol appears to temporarily impede the functioning of the receptors, causing a short-term increase in appetite.

Leptin is important in the regulation of fat mass and body weight. Adipose tissue (fat cells) not only secretes leptin, but also serves as a site of action for leptin through the cell surface receptors. Leptin receptors exist in at least four forms on the surface of cells, a single major isoform and three smaller isoforms. Recent studies indicate that the smaller leptin receptor isoforms play the most important role in body weight control.

Leptin plays a significant role in mammalian physiology and, thus, may be found in association with patho-physiological conditions. Because of the involvement of leptin in the regulation of body weight, the level of leptin in the serum is considered to be one of the best biological markers of body fat in both humans and animals. Obesity in humans is accompanied by an increased level of leptin in the circulation. There are also gender differences in the observed levels of leptin in the blood associated with body mass. Leptin levels are correlated with those of a number of endocrine substances such as insulin, glucocorticoids, thyroid hormones and testosterone. Recent studies also indicate that it may be involved in mediating some endocrine-related mechanisms, like the onset of puberty, and impaired or modified receptor functions may be associated with certain medical conditions, such as obesity, polycystic ovary syndrome, sleep apnea, cardiovascular disease and certain types of cancer and the wasting associated with the disease. Research findings also indicate that leptin can act as a growth factor in the fetus and in the neonate.

Obesity results from an imbalance between caloric energy and energy expenditure. Genetic factors play an important role in its pathogenesis. Several single-gene defects responsible for obesity have been identified. Leptin is the most notable example of such a gene defect, but a number of other proteins and neuropeptides have also been shown to participate in a complex network that regulates food intake and energy expenditure. In obesity, one of the most significant changes is the shift from small adipocytes to large adipocytes with a concomitant reduction in leptin production per cell. Further, it has been shown that the leptin receptor population on the large fat cells shifts primarily to the larger isoform and that their functioning is impaired when compared to the receptors found on adipocytes in non-obese individuals. The result is more leptin backed-up in the circulation with a failure to send the signals that would suppress appetite and increase metabolism. This is further complicated by dietary factors. For example, it has been shown that exposure of leptin receptors to a variety of fatty acids results in significant impairment of their ability to bind leptin.



The colostrum powder produced by Immuno-Dynamics evidences a consistently high level of leptin in each manufactured serial.

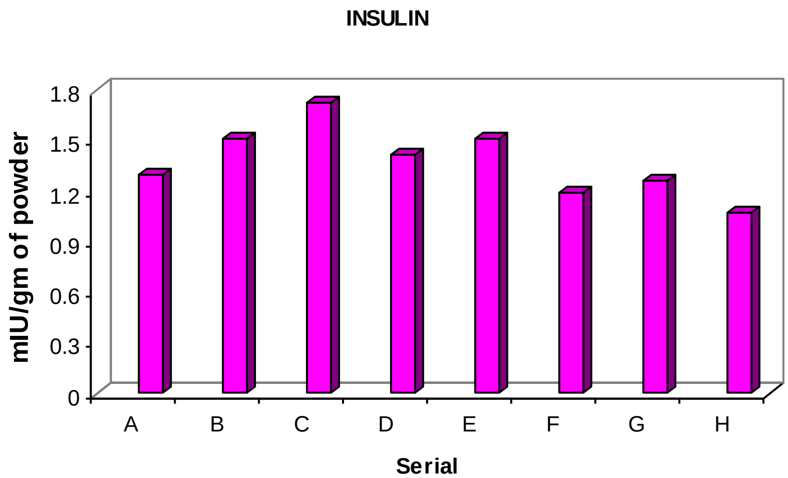
- **Insulin**

Insulin is a small peptide hormone produced in the Islets of Langerhans of the pancreas. It regulates the metabolism of carbohydrates, fats and starches in the body. The body normally converts glucose to glycogen to derive the metabolic energy needed for the maintenance of vital functions. This process is initiated by the binding of insulin to cell surface receptors that are very specific for the molecular configuration of that hormone. This triggers a cascade of events that includes the binding of IGF-1 and leptin to their specific receptors. Thus, there is a strong metabolic inter-dependence between the functions of insulin, IGF-1 and leptin that influences the metabolism of carbohydrates and fats and the derivation of the metabolic energy necessary to support bodily functions.

If the pancreas produces too little insulin and/or the interaction of insulin with its cell surface receptors is impaired, the amount of sugar in the blood increases, producing a condition known as hyperglycemia. This condition, in itself, is not lethal, but is a symptom of a serious disease, diabetes mellitus. Diabetes mellitus is usually classified into two types. Type I is called insulin-dependent diabetes mellitus (IDDM) and was previously known as juvenile-onset diabetes since it occurs primarily in children and young adults. It accounts for about 10-15 percent of all cases of diabetes and can progress very rapidly. Type II is called non-insulin-dependent diabetes mellitus (NIDDM) and was formerly known as adult-onset diabetes since it usually occurs in persons over 40 years old. This form of diabetes progresses very slowly and affected individuals often have no outward signs of clinical illness, but, rather, are detected by the presence of elevated blood and/or urine glucose levels.

In the Type I diabetic, the problem is almost always associated with a severe reduction in the amount of insulin produced, while, in the Type II diabetic, the pancreas makes sufficient insulin, but the hormone cannot promote the entry of glucose into cells. The high level of blood sugar then inactivates the receptors for insulin that would normally be functional on the surface of the cells. In some individuals, the development of Type II diabetes seems to be associated with prolonged obesity. Both Type I and II diabetes have an associated genetic component through which individuals appear to be predisposed and they also have low levels of IGF-1 in their circulation.

Insulin ordinarily is ineffective when administered by mouth since it is rapidly degraded by proteolytic enzymes in the stomach. However, at least two factors associated with the delivery of insulin in complete bovine colostrum likely support its absorption into the body in a functional form. First, colostrum contains trypsin inhibitors and it has been shown that trypsin, a proteolytic enzyme, is primarily responsible for the degradation of insulin in the stomach and that the addition of trypsin inhibitors to orally administered insulin enhances its absorption into the body. In addition, when colostrum is ingested, the casein and fat are acted upon by another enzyme in the stomach, rennin, forming a cottage cheese-like curd that serves to protect the biologically active components from the effects of stomach acid and enzymes, allowing them to pass intact into the small intestine, where they are absorbed.



As with the associated components, IGF-1 and leptin, the colostrum powder produced by Immuno-Dynamics evidences a consistently high level of insulin in each manufactured serial.

- **Lactoferrin**

Lactoferrin is a single-chain metal-binding glycoprotein with a molecular weight of about 78,000 daltons. It is present in large quantities in both human and bovine colostrum and, to a lesser extent, in both human and cow’s milk, as well as in other exocrine secretions. A great deal of structural information has been developed about the lactoferrin molecule and it has been possible to relate this information to three significant properties of lactoferrin; a) its ability to bind a wide variety of metal ions with extremely high affinity; b) its ability to bind cations; and c) its ability to bind to a number of different cell types.

Lactoferrin has the capacity to reversibly bind two iron (Fe) ions concomitantly with two carbonate (CO3=) or bicarbonate (HCO3-) anions. The features of metal binding by lactoferrin that are particularly significant include the synergistic relationship between cation and anion binding, the extremely tight binding of iron, and the existence of mechanisms for the release of tightly bound iron. Other metals of similar size and charge can be substituted for iron in the two specific binding sites.

In colostrum, as in other secretions, lactoferrin is mostly iron-free, with a saturation level of about 8-10%. In this iron-free form, it has very pronounced bacteriostatic properties, probably dependent upon its ability to bind adventitious iron very tightly, thus depriving certain bacteria, like *E. coli,* of iron that is essential for their growth. In addition, sequestration of iron by lactoferrin restricts iron-catalyzed free radical damage to cells.

The ability of lactoferrin to bind to a variety of normal and leukemic blood cells has led to the suggestion that the lactoferrin released by neutrophils plays a role in modulating immune and inflammatory responses. Lactoferrin promotes the aggregation of neutrophils and their adhesion to epithelial cells, suggesting that lactoferrin may be the agent that causes neutrophils to accumulate at the site of inflammation.

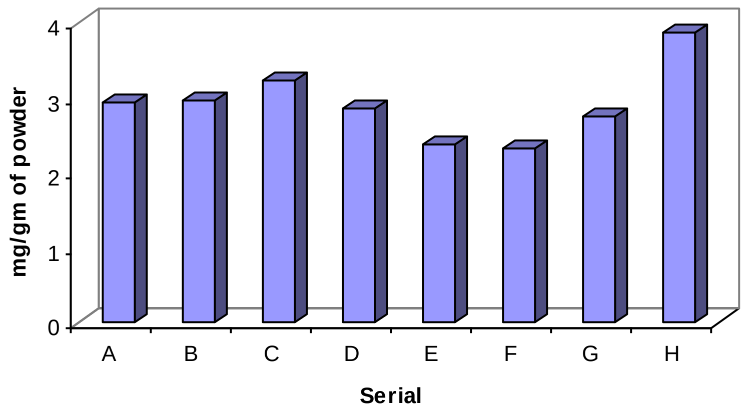
The lactoferrin molecules derived from different tissues and secretions appear to be identical in structure and function, eg the DNA sequence of lactoferrin from leukocyte granules matches the amino acid sequence of the lactoferrin found in colostrum and milk. Lactoferrin isolated from various mammalian species has also been found to be essentially identical in both structure and function.

Biologically Active Components

Beta-Lactoglobulin, Lactoferrin
(mass/gm of powder)

Serial	Lactoferrin (mg/gm)	Beta-Lactoglobulin (mg/gm)
A	2.927	17.936
B	2.950	19.545
C	3.211	19.555
D	2.840	19.164
E	2.379	21.064
F	2.318	23.545
G	2.740	24.836
H	3.859	22.891
Mean	2.903	21.064
S.D.	0.487	2.441
95% Int	0.974	4.882
Range	1.929 - 3.877	16.182 -25.946

LACTOFERRIN



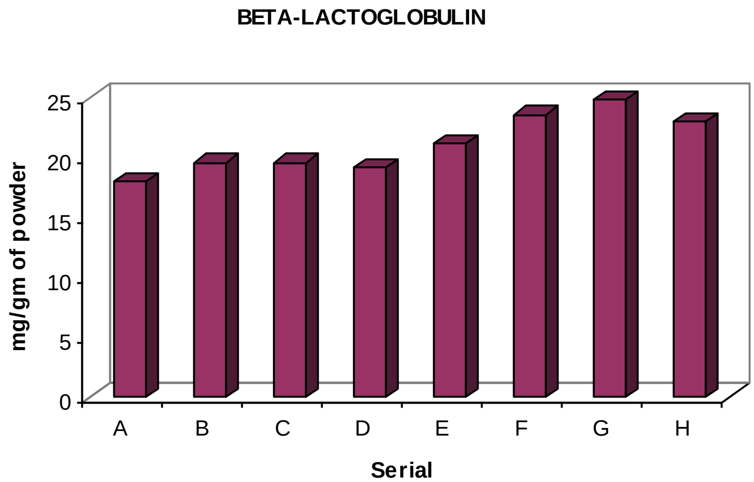
The colostrum powder produced by Immuno-Dynamics consistently evidences levels of lactoferrin above 2.5mg per gram in each manufactured serial.

- **Beta-Lactoglobulin**

Beta-lactoglobulin compromises about 10% of milk protein and is the most prevalent protein in whey, representing about 50-60% of the protein content. It has a molecular weight of about 18,300 daltons and contains 162 amino acids. The molecular structure of beta-lactoglobulin has been extensively studied and it has been shown that there are two genetic variants, A and B, that differ in the substitution of a glycine in Variant B for an aspartic acid in Variant A. Below pH 3 and above pH 8, beta-lactoglobulin exists as a monomeric structure, while between pH 3.1 and 5.1 at low temperatures and high protein contents, it self-associates to form an octamer. At other pH values, including the pH of milk, beta-lactoglobulin tends to be found as a spherical dimer, which has a solubility of about 50 mg/ml in milk. It has been shown that the heat treatment of milk can result in the binding of up to four lactose molecules to each beta-lactoglobulin molecule.

Beta-lactoglobulin is manufactured in the mammary gland and is expressed in the mammary gland during pregnancy and lactation. All colostrum and milk from ruminants contains beta-lactoglobulin while the milk from most non-ruminants does not. However, it is found to a lesser extent in the milk from horses, dogs, dolphins and whales.

The primary role of beta-lactoglobulin is as a transporter of small linear fatty acid-like hydrophobic molecules, which is a large group of substances that binds molecules such as retinol (vitamin A), triglycerides and fatty acid-synthesis and -breakdown intermediates. The molecular structure of beta-lactoglobulin is unique, consisting of eight non-parallel strands of amino acids with a channel in the center that coils around on itself to form a hydrophobic unit where transported molecules are inserted.



The colostrum powder produced by Immuno-Dynamics evidences consistent and substantial levels of beta-lactoglobulin as would be characteristic of a high quality first milking bovine colostrum.

- **Thymosin alpha-1; Thymosin beta-4**

The thymus gland, located over the sternum, is an endocrine organ for which a unified, physiological concept of humoral regulation of the immune response has emerged in recent years. The thymus gland is the major site for maturation of immuno-competent T lymphocytes from their hematopoetic stem cells. This very complex process requires direct cell-to-cell receptor-based interactions, as well as specialized chemical signals via the numerous cytokines and thymic hormones produced by cells in the thymus. Thymic hormones are polypeptides that have been shown to localize in the reticulo-endothelial cells of the thymus. The complex maturation sequence of T lymphocytes and the derivation of numerous unique subpopulations of these cells involves the orchestral interaction of various thymic-specific factors, including the hormone thymosin, and other molecules during the differentiation process.

Thymosin fraction 5 and its constituent hormone-like peptides, thymosin alpha-1 and thymosin beta-4, influence several properties of lymphocytes including cyclic nucleotide levels, migration inhibitory factor production, T-cell dependent antibody production, as well as expression of various cell surface maturation and differentiation markers. In various clinical trials, these thymic hormones have been shown to strengthen the effects of immuno-modulators in immuno-deficiencies, autoimmune diseases and neoplastic malignancies.

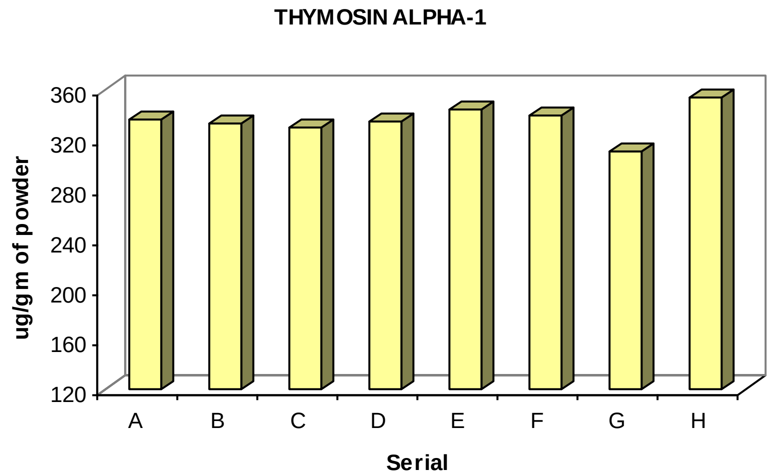
Thymosin alpha-1 is a small peptide with a molecular weight of approximately 5,000 daltons. It has been shown to enhance the maturation of undifferentiated stem cells into disease-fightting T-cells and to enhance the production of cell messengers that coordinate the complex response of the immune system to disease. More recent studies have also shown that thymosin alpha-1 directly increases the immune system's ability to recognize and target cancerous and virus-infected cells among healthy cells.

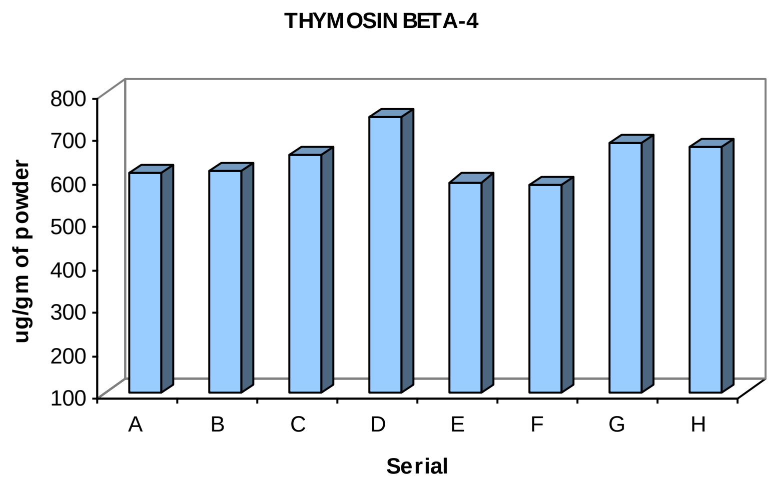
Thymosin beta-4 is part of a family of beta thymosin peptides each having a molecular weight of about 5,000 daltons. The beta thymosins are present in varying concentrations in almost every cell in the body. They bind monomeric actin in a 1:1 complex and act as buffers, preventing polymerization into actin filaments, but supplying a pool of actin monomers when a cell needs filaments for differentiation. Thymosin beta-4 is also present outside of cells in blood plasma and in wound fluid. It has been shown to influence the induction of certain enzymes, the migration of white blood cells through tissues and the rate of cell differentiation. Thymosin beta-4 has also been shown to inhibit inflammation and to limit stem cell differentiation from bone marrow.

Biologically Active Components

Thymosin alpha-1, Thymosin beta-4
(mass/gm of powder)

Serial	Thymosin alpha-1 (ug/gm)	Thymosin beta-4 (ug/gm)
A	335.45	611.82
B	332.82	617.82
C	329.64	652.73
D	333.55	742.27
E	344.00	591.91
F	338.27	585.45
G	310.73	681.64
H	353.64	673.64
Mean	334.73	644.636
S.D.	12.326	53.301
95% Int	24.652	106.602
Range	310.075 - 359.379	538.034 - 751.238





The colostrum powder manufactured by Immuno-Dynamics consistently contains high levels of both thymosin alpha-1 and thymosin beta-4.

- **Immunoglobulins**

The formation of colostrum starts 3-4 weeks before the birth of the calf, when hormonal changes trigger the activation of sites within the mother's mammary glands. When fully activated, these sites begin to transfer biologically-active substances into the mammary gland where colostrum is formed. It is through this mechanism alone that antibodies (specifically immunoglobulins of the IgG class), from the mother's blood enter into the mammary gland. Specialized white blood cells from the mother are also transferred in the same way. These cells immediately begin to release other immunoglobulin molecules (IgM and IgA) into the developing colostrum.

Antibodies have some specialized functions, partly due to the "Y" shape of these long-chain proteins. The arms of the Y can attach to an antigen and, once this happens, the tail of the Y unfolds. This tail region differs among the five main classes of immunoglobulins (IgM, IgG, IgA, IgD and IgE). For example, IgM molecules have very short tail pieces which are used to connect five Y molecules together creating a big molecule with ten possible sites where it can attach itself to a microorganism. All of the other classes represent molecules that are about one-third as big as IgM, but are much more effective.

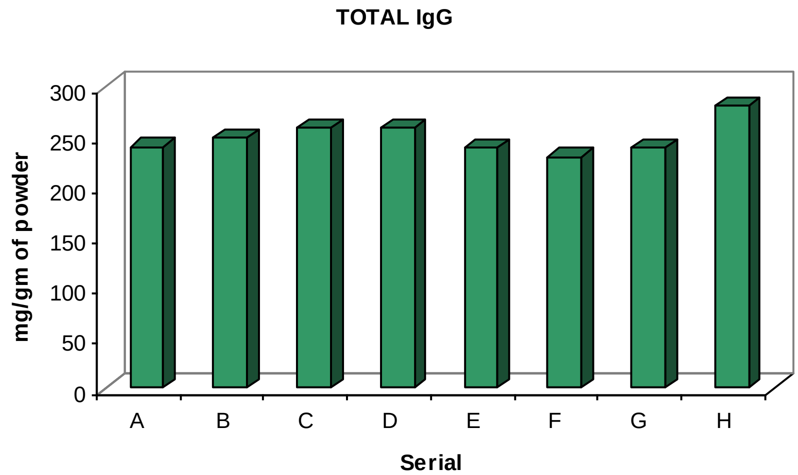
IgM and IgG classes of antibodies function best when they are in the bloodstream. In contrast, immunoglobulins of the IgA class can operate in the bloodstream or in other bodily fluids like the tears and saliva. IgA molecules can also be found in the lungs and intestines. Here, the tails attach to mucous membranes so the arms of the molecule can “catch” and immobilize invading organisms. Since most infectious agents enter the body through the respiratory or digestive pathways, IgA is very important in resisting many infections.

The antibodies in orally ingested bovine colostrum do not enter the bloodstream, except through a specialized mechanism in newborn calves. However, these antibodies have been shown to be effective in enteric infections in various species. This is because dairy cows are repeatedly exposed to most of the same bacteria and viruses that cause enteric infections in other mammals, including humans, (Escherichia coli, Staphylococcus species, Salmonella species, rotavirus, etc.). Thus, in addition to assuring that the colostrum used is only from a first milking taken during the first six hours after birth, it is important to utilize a colostrum product with a high degree of "antibody diversity." This means that it has been collected from many cows on a lot of different dairy farms and potentially provides protection against a broad number of microorganisms.

Biologically Active Components

Immunoglobulin G (IgG)
(mass/gm of powder)

Serial	IgG1 (mg/gm)	IgG2 (mg/gm)	Total IgG (mg/gm)
A	232.40	8.79	241.19
B	239.20	10.81	250.01
C	248.40	10.92	260.32
D	248.40	10.92	260.32
E	230.00	10.35	240.35
F	220.80	10.35	231.15
G	230.00	10.47	240.47
H	271.40	10.81	282.21
Mean	240.075	10.428	250.753
S.D.	15.830	0.704	16.313
95% Int	31.660	1.408	32.626
Range	208.415 - 271.735	9.02 - 11.836	218.127 - 283.379



The colostrum powder produced by Immuno-Dynamics evidences a uniform, consistently high level of immunoglobulin G (IgG) in each serial manufactured.

CHARACTERIZATION OF COLOSTRUM PRODUCTS

COMPETITORS

Basic Chemical Composition

As discussed earlier, the best way to determine the basic quality of a colostrum product is to establish the relationship of three major components, protein, fat and lactose, a relationship that changes with time after birth of the calf. The basic chemical composition eight (8) colostrum powder products from different manufacturers is compared with the mean values for ten (10) serials manufactured from large pools by Immuno-Dynamics in the following table. The same data is also graphically displayed. Comparison of these data with the values given in the table from the Handbook of Dairy Chemistry shown earlier and again below indicates a) whether the products employ colostrum collected within six (6) hours after birth of the calf in a single milking; and whether the colostrum has been altered, potentially reducing its effectiveness.

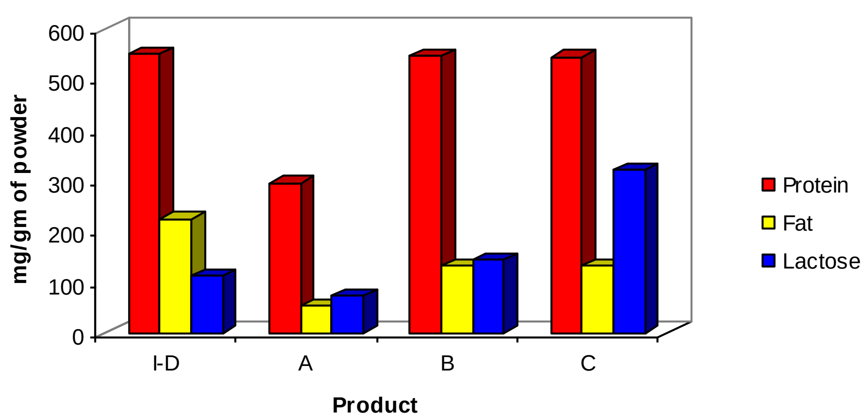
Composition of Bovine Colostrum
(mg/gm of total solids)

Hours After Birth	Total Protein	Fat	Lactose
0	651.0	189.0	811.0
6	489.0	334.8	132.5
12	416.4	261.5	255.3
24	354.0	266.2	311.7

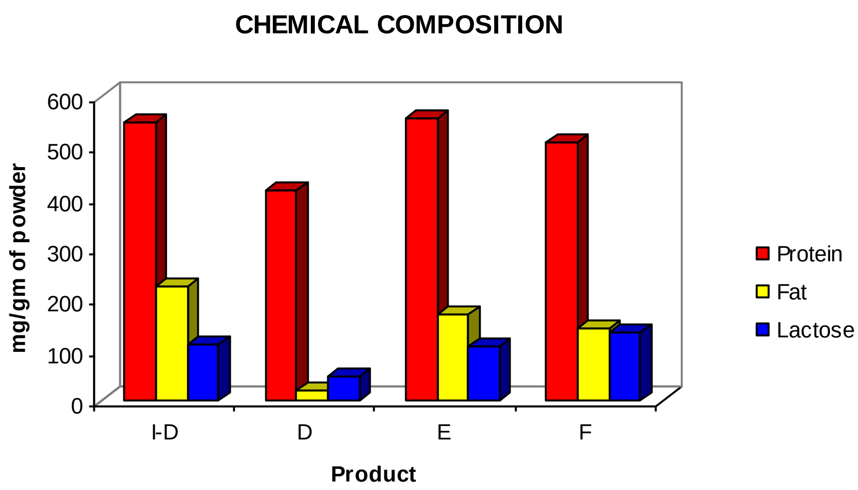
Since the data shown earlier substantiated that the colostrum powder products manufactured by Immuno-Dynamics meet the criteria for a high quality first milking colostrum collected within six (6) hours after birth, the mean values for these products will be used as a benchmark for comparison to establish the relative quality of the tested competitor products. In all cases, a letter designation for an individual product represents the same product in all tables and graphs.

CHEMICAL COMPOSITION
(mg/gm of powder)

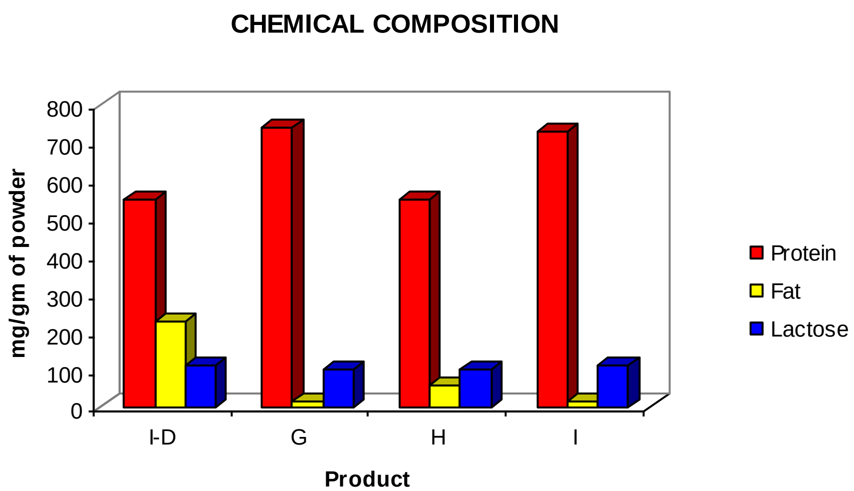
Product	Total Protein	Total Fat	Total Lactose
I-D	**549.7**	**224.5**	**111.3**
A	295.8	53.9	74.0
B	518.6	131.1	144.0
C	545.1	133.0	322.0
D	413.0	19.2	48.0
E	557.1	170.9	106.0
F	508.4	140.9	134.0
G	740.0	12.4	97.0
H	547.5	53.5	100.0
I	730.1	11.8	108.0



Comparison of the composition of Product A with that of the Immuno-Dynamics' (I-D) products indicates that it is deficient in protein content with the value being indicative of colostrum collected more than 24 hours after birth. The very low fat content of this product indicates that it have been adulterated by partial removal of the fat during processing. Since lactose is produced by cells in the mammary gland and rises with time after birth, the exceedingly low level of lactose in Product A is indicative of further adulteration with substantial removal of the lactose. The level of fat found in Product B is below that expected for colostrum collected 6 hours after birth, indicating that some of it has been removed and the lactose level is higher than normal indicating that the colostrum used was collected more than 6 hours after birth. The fat content of Product C indicates that some of this material has been removed, which artificially causes an increase in observed protein and lactose values since the determinations are based upon total solids. Adjusted values for this adulterated product indicate that the colostrum used was collected between 6-12 hours after birth.



The compositional analysis for Product D also indicates that the fat and a major portion of the lactose were removed during processing. Adjustment of the protein content for this adulteration indicates that the colostrum used to produce this product was collected more than 24 hours after birth. The basic chemical composition of Products E and F is similar to that of Immuno-Dynamics' colostrum powder although the fat content is somewhat lower, a characteristic that can occur in colostrum collected within 6 hours after birth.



Products G, H and I have been adulterated by removal of the fat with that component being almost completely removed from Products G and I. This would artificially inflate both the protein and lactose levels and, since the lactose level in these products is lower than would be expected, it indicates that some of that component has been removed from each of the products. The adjusted protein values for Products G and I indicate that they employed colostrum collected more than 24 hours after birth, while the adjusted protein value for Product H indicates the use of colostrum collected up to 24 hours after birth.

Biologically Active Components

As for the testing conducted with the serials produced by Immuno-Dynamics, a series of eight (8) of the biologically active components of bovine colostrum were selected as the marker components based upon a) the availability of an immunoassay for the determination of concentration; b) the ability of the assay or an adaptation thereof to perform reliably with colostrum; an c) **the importance of the role of the component in the biological effects observed with colostrum**. The assays were conducted by the diagnostic laboratory at a major college of veterinary medicine.

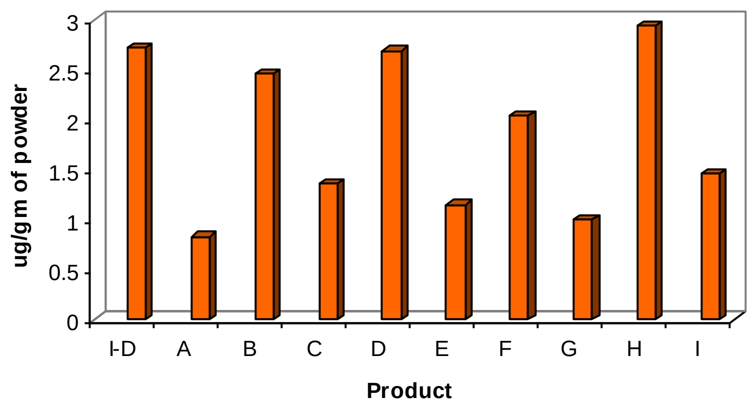
In this case, colostrum powder products from nine (9) different manufacturers were evaluated. Again, in all cases, a letter designation for an individual product represents the same product in all tables and graphs.

BIOLOGICALLY ACTIVE COMPONENTS

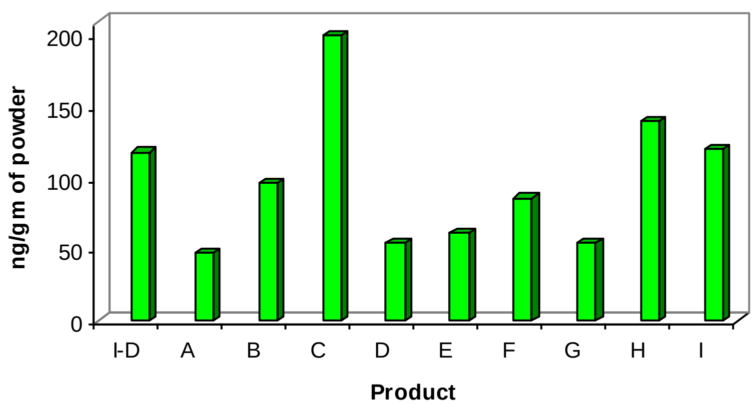
IGF-1, Leptin, Insulin

Product	IGF-1 (ug/gm)	Leptin (ng/gm)	Insulin (mIU/gm)
I-D	**2.723**	**118.45**	**1.375**
A	0.827	47.72	0.931
B	2.455	96.21	1.239
C	1.357	200.41	4.713
D	2.688	54.91	0.060
E	1.147	61.39	0.513
F	2.046	85.89	0.915
G	1.004	54.25	0.397
H	2.943	139.62	1.412
I	1.461	120.75	1.991

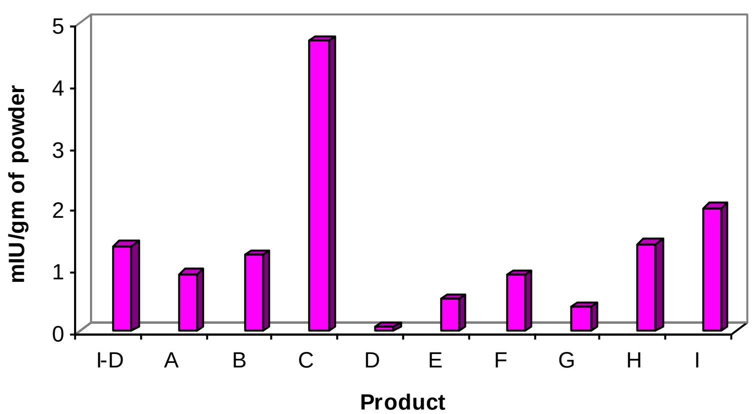
INSULIN-LIKE GROWTH FACTOR



LEPTIN



INSULIN



Comparison of the IGF-1, leptin and insulin content of Product A with that of the products from Immuno-Dynamics indicates that this product is significantly deficient in those components, which is not surprising since the compositional data indicated that the colostrum used to manufacture the tested product was a) collected more than 24 hours after birth; and b) had been adulterated by removal of both fat and lactose.

Product B had normal levels of total protein that would ordinarily be found in a high quality first milking bovine colostrum collected within 6 hours after birth, but had a reduced fat content and elevated lactose. However, its IGF-1, leptin and insulin contents were consistent with a colostrum collected within 6 hours after birth.

The compositional analysis indicated that a portion of the fat had been removed from Product C, artificially inflating the protein value. In addition, the data showed that the colostrum used to produce the powder had been collected between 6-12 hours after birth. Accordingly, the product evidences a reduced content of IGF-1, which is partially fat soluble, and substantially increased leptin and insulin values, a phenomenon associated with the artificial increase in protein content.

Product D was also shown to have a markedly reduced fat content in the compositional analysis and the adjusted values indicated that the colostrum used was collected more than 24 hours after birth. The product evidences a markedly reduced leptin level and it was essentially devoid of any insulin. In contrast, the product had essentially normal IGF-1 levels in comparison to the powder produced by Immuno-Dynamics. Insulin is almost completely removed by the formation of a curd in the production of whey, leaving the residual IGF-1 and leptin essentially intact, but artificially inflating their content by the removal of other major components. Thus, the assayed values derived with Product D are characteristic of dried whey.

Although Product E was thought to have a chemical composition essentially like that seen with the powder products manufactured by Immuno-Dynamics, its IGF-1, leptin and insulin content are considerably lower. As with Product B, this discrepancy may be the result of using highly diverse collection schedules and, in some cases, pools from multiple milkings in assembling the large pool of “colostrum” used to manufacture the powder tested.

Product F also evidenced a chemical composition similar to that seen with the powder products manufactured by Immuno-Dynamics. This product demonstrated considerably higher levels of IGF-1, leptin and insulin than Product E, but still somewhat lower than those found with Immuno-Dynamics’ products. These lower values indicate that the colostrum pool used to produce the powder may have utilized some materials collected after the 6-hour period and combined them with higher quality material.

The compositional analysis for Product G indicated that it was adulterated by removal of fat and lactose and that it employed colostrum collected more than 24 hours after birth. These observations were verified by the very low levels of IGF-1, leptin and insulin found in the tested powder.

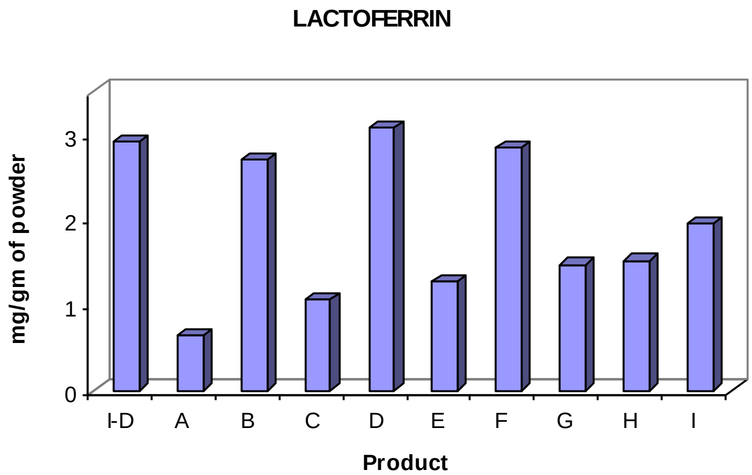
The compositional analysis for Product H indicated that almost all of the fat and most of the lactose had been removed resulting in an artificially elevated protein content, which also resulted in elevated levels of IGF-1, leptin and insulin in the assayed powder. In contrast to the values obtained with Product C, which was apparently adulterated in a similar fashion, the content of all three components was uniformly elevated. Therefore, it would appear that a method was used for fat and lactose removal that did not alter the IGF-1 content of the colostrum.

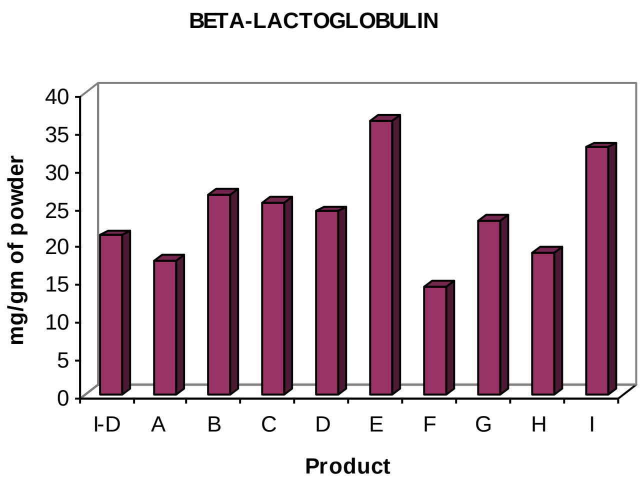
Product I evidences a reduced IGF-1 content, a normal leptin concentration and a somewhat elevated amount of insulin. The results of these assays are characteristic of a product that employed colostrum collected up to 24 hours after birth, perhaps from multiple milkings, and adulterated by removal of all or some of the fat using a method that removed the fat-soluble portion of the IGF-1. This would result in an artificial increase in the values for the remaining components.

BIOLOGICALLY ACTIVE COMPONENTS

Lactoferrin, Beta-Lactoglobulin

Product	Lactoferrin (mg/gm)	Beta-Lactoglobulin mg/ml
I-D	**2.903**	**21.064**
A	0.646	17.680
B	2.689	26.529
C	1.053	25.454
D	3.069	24.233
E	1.268	36.200
F	2.837	14.295
G	1.471	23.136
H	1.517	18.724
I	1.955	32.711





Comparison of the lactoferrin and beta-lactoglobulin content of Product A with that of the products from Immuno-Dynamics indicates that this product contains very little lactoferrin and a substantially reduced quantity of beta-lactoglobulin. The proportionally higher quantity of beta-lactoglobulin is likely due to the fact that the colostrum used was collected more than 24 hours after birth and bovine milk contains a substantial quantity of this component.

Product B evidenced essentially the same levels of lactoferrin and beta-lactoglobulin observed with the powder produced by Immuno-Dynamics. However, approximately half of the fat has been removed from the colostrums, which would artificially inflate these values.

Product C assay values indicated a reduced lactoferrin concentration with a normal quantity of beta-lactoglobulin. The reduced lactoferrin concentration is consistent with use of colostrum collected 6-12 hours after birth since lactoferrin is transferred from the mother' circulation during late gestation and is not produced by cells in the mammary gland. In contrast, beta-lactoglobulin is only produced by cells in the mammary gland and its content increases with time after birth, which could result in a normal-appearing value with late collection materials.

Earlier data indicated that Product D is dried whey with normal IGF-1 levels, but low leptin content and essentially no insulin. The normal lactoferrin and beta-lactoglobulin levels, in comparison to the Immuno-Dynamics' products, are also consistent with a dried whey-based product.

Consistent with observed low levels of IGF-1, leptin and insulin in Product E, low levels of lactoferrin were also seen. However, the product evidenced an extremely high content of beta-lactoglobulin. These characteristics are all indicative of a product that employs colostrum collected at least 24 hours after birth from multiple milkings. In this case, the primary biologically active components would be significantly diluted by transitional milk with a concomitant increase in beta-lactoglobulin, which is an inherent component of bovine milk.

Product F evidenced a normal level of lactoferrin and a somewhat reduced concentration of beta-lactoglobulin in comparison to the values found with the powder produced by Immuno-Dynamics. The observed values are consistent with a product that employs colostrum pools that employ diverse materials, much of which was collected during the first 6 hours after birth, as was concluded for the IGF-1, leptin and insulin determinations.

The reduced level of lactoferrin and seemingly normal level of beta-lactoglobulin observed with Product G are consistent with a product that used colostrum collected more than 24 hours after birth and was adulterated by removal of the fat and lactose. This further verifies the same conclusion drawn from the compositional analysis and the results of assays for IGF-1, leptin and insulin content.

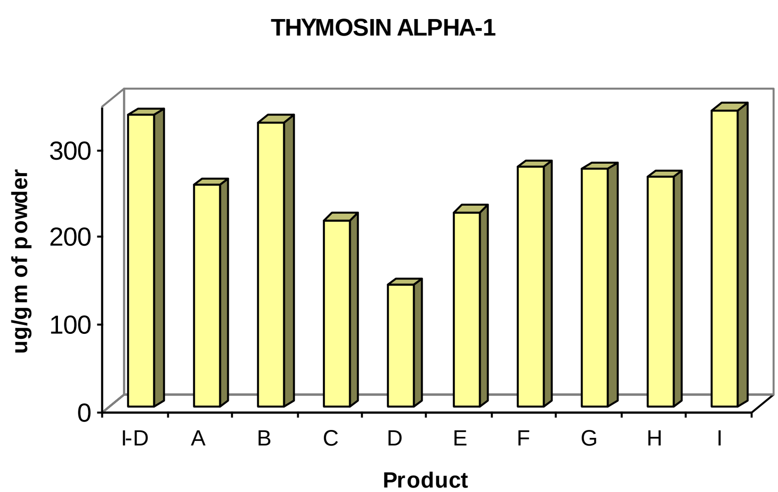
Although Product H evidenced elevated IGF-1, leptin and insulin levels, despite having the fat removed, its lactoferrin level was below that seen with the Immuno-Dynamics' products. In addition, the beta-lactoglobulin content was slightly lower than normal. The combined characteristics for this adulterated product are indicative of one that has been selectively manipulated. Removal of the fat should have resulted in artificial elevation of the content for all measured proteins, but this occurred only for some selected components.

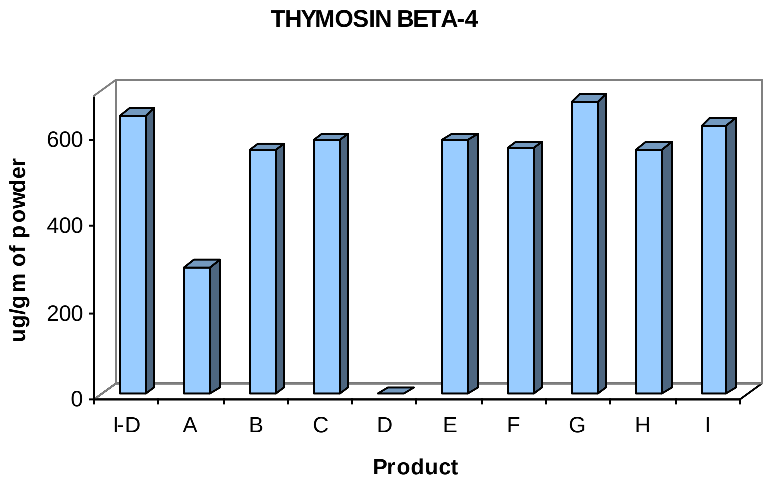
Product I evidences a reduced quantity of lactoferrin with an increased level of beta-lactoferrin. This is consistent with the use of colostrum collected at least 24 hours after birth and further supports the same conclusion derived with the IGF-1, leptin and insulin values.

BIOLOGICALLY ACTIVE COMPONENTS

Thymosin alpha-1, Thymosin beta-4

Product	Thymosin alpha-1 (ug/gm)	Thymosin beta-4 (ug/gm)
I-D	**334.727**	**644.636**
A	254.795	295.000
B	326.491	565.909
C	214.382	586.818
D	138.750	BDL
E	223.486	586.364
F	274.218	569.545
G	272.959	678.182
H	262.641	566.818
I	339.836	622.273





Comparison of the thymosin alpha-1 and thymosin beta-4 content of Product A with the powder products from Immuno-Dynamics indicates that this product contains a significantly lesser amount of thymosin alpha-1 and a markedly lower quantity of thymosin beta-4. As with the previous findings, these values are consistent with the use of colostrum that was collected more than 24 hours after birth.

Product B evidenced thymosin alpha-1 and thymosin beta-4 levels consistent with the range of values observed with the powder produced by Immuno-Dynamics, which is the same conclusion reached for the values obtained with each of the other tested constituents. The combined findings are indicative of the use of colostrum collected at the first milking within 6 hours after birth.

The compositional analysis indicated that a portion of the fat had been removed from Product C, artificially inflating the protein value. In addition, the data showed that the colostrum used to produce the powder had been collected between 6-12 hours after birth. Accordingly, the product evidences a reduced value for thymosin alpha-1 and a normal level of thymosin beta-4. However, these values are likely artificially inflated, due to removal of the fat, as was observed for leptin and insulin.

Product D evidences a very low level of thymosin alpha-1 and no detectable thymosin beta-4. The reduced levels are consistent with the use of colostrum collected more than 24 hours after birth. However, previous data indicates that the product is dried whey and it is not known what effect the generation of whey from colostrum would have on the concentration of these constituents although the results imply that most of the thymosin beta-4 is removed.

Again consistent with observed lower levels of IGF-1, leptin, insulin and lactoferrin, Product E exhibited low levels of thymosin alpha-1. However, as with beta-lactoglobin, the product also exhibited thymosin beta-4 levels within the normal range. Although it is uncertain as to why the thymosin beta-4 value would appear normal, the rest of the characteristics are consistent with a product that employs colostrum collected at least 24 hours after birth.

Product F evidenced both thymosin alpha-1 and thymosin beta-4 values that were just outside of the range of values seen with the powder products produced by Immuno-Dynamics. These findings are consistent with previous observations for the other constituents and are also indicative of the use of colostrum pools that employ diverse materials, much of which was collected during the first 6 hours after birth.

Product G evidenced thymosin alpha-1 at a level just below the normal range and a normal level of thymosin beta-4. Data for the other constituents was consistent with the use of colostrum obtained more than 24 hours after birth and the compositional analysis demonstrated that the product was adulterated by removal of fat and lactose. The seemingly normal levels of thymosin alpha-1 and thymosin beta-4 may be a manifestation of fat removal and the associated artificial increase in protein content.

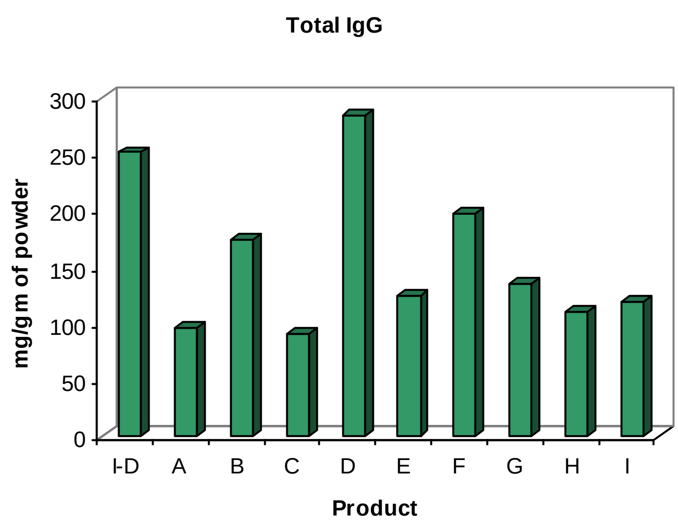
The thymosin alpha-1 and thymosin beta-4 values for Product H were just below the range of values seen with the powder products produced by Immuno-Dynamics. This product evidenced a unique profile for the biologically active components, elevated IGF-1, leptin, insulin levels with lower than normal values for lactoferrin, beta-lactoglobulin, thymosin alpha-1 and thymosin beta-4. In addition, the compositional analysis showed that the fat had been substantially removed. This product may have been uniquely manipulated during processing and/or it used colostrum collected more than 24 hours after birth, which originally had a low content of active components that were substantially elevated by removal of almost all of the fat.

Product I contained essentially normal levels of thymosin alpha-1 and thymosin beta-4. Results from the assays for other constituents evidenced reduced concentrations of some components and were consistent with the use of colostrum collected up to 24 hours after birth, which was not the case for either of the thymosins. However, the results indicated a low level of IGF-1 in this product. Since IGF-1 is partially fat soluble and its concentration is usually lowered when the fat is removed from colostrum, it is possible that the fat was totally or partially removed from the colostrum used to manufacture the powder. This would artificially elevate the levels of the remaining protein constituents and could explain the results observed here. Unfortunately, the chemical composition of this product was not determined.

BIOLOGICALLY ACTIVE COMPONENTS

Immunoglobulin G (IgG)

Product	IgG1 (mg/gm)	IgG2 (mg/gm)	Total IgG (mg/gm)
I-D	**240.075**	**10.428**	**250.753**
A	92.00	4.72	96.72
B	165.60	7.71	173.31
C	87.40	3.45	90.85
D	271.40	12.40	283.80
E	119.60	5.17	124.77
F	188.00	9.20	197.20
G	105.8	5.06	110.86
H	115.00	4.37	119.37
I	131.10	4.60	135.70



Comparison of the Immunoglobulin G (IgG) content of Product A with that of the products from Immuno-Dynamics indicates that this product is significantly deficient in this component, which is not surprising since the compositional data indicated that the colostrum used to manufacture the tested product a) was collected more than 24 hours after birth and the transfer of IgG into colostrum ceases at birth; and b) had been adulterated by removal of both fat and lactose.

Product B had a level of total protein that would normally be found in a high quality first milking bovine colostrum collected within 6 hours after birth, but some of the fat had been removed, which would artificially inflate the other values. Despite this effect, its IgG content was lower than that observed with Immuno-Dynamics' products, indicating that the colostrums was collect beyond the desirable 6-hour period.

The compositional analysis indicated that a portion of the fat had been removed from Product C, artificially inflating the protein value. In addition, the data showed that the colostrum used to produce the powder had been collected between 6-12 hours after birth. Accordingly, the product evidences a substantially reduced content of IgG.

Product D was also shown to have a markedly reduced fat content in the compositional analysis and the adjusted values indicated that the colostrum used was collected more than 24 hours after birth. The assayed values derived with Product D for the various biologically-active components are characteristic of dried whey and the product evidences an artificially inflated amount of IgG.

Although Product E was thought to have a chemical composition essentially like that seen with the powder products manufactured by Immuno-Dynamics, its IgG content is considerably lower, as were the values for IGF-1, leptin and insulin. These discrepancies may be the result of manipulation during the manufacturing process or it may be due to the use of colostrum with highly diverse collection schedules and, in some cases, pools from multiple milkings in assembling the large pool of "colostrum" used to manufacture the powder tested.

Product F also evidenced a chemical composition similar to that seen with the powder products manufactured by Immuno-Dynamics. This product demonstrated a considerably higher level of IgG than Product E, but still somewhat lower than that found with Immuno-Dynamics' products. The lower value indicates that the colostrum pool used to produce the powder may have utilized some materials collected after the 6-hour period and combined them with higher quality material.

The compositional analysis for Product G indicated that it was adulterated by removal of fat and lactose and that it employed colostrum collected more than 24 hours after birth. These observations were verified by the lower level of IgG found in the tested powder.

The compositional analysis for Product H indicated that almost all of the fat and most of the lactose had been removed resulting in an artificially elevated protein content, which also resulted in elevated levels of IGF-1, leptin and insulin in the assayed powder. However, this did not artificially increase the low level of IgG in the product indicating that the powder was produced from "colostrum" obtained in multiple milkings taken up to 48 hours after birth.

Product I also evidences a reduced IGF-1 content. The chemical composition of this product indicated that the it was adulterated by removal of most of the fat. The results of the other assays are characteristic of a product that employed colostrum collected up to 24 hours after birth, perhaps from multiple milkings.

Summary of Observations

The following table provides a direct comparison of all competitor products tested with the mean values for the chemical composition and biologically active components observed with ten (10) serials of powder manufactured by Immuno-Dynamics. In all cases, the mean values for the Immuno-Dynamics' products are used as the baseline and, for comparative purposes, the values for each product are expressed as a percent (%) of the mean observed value for the Immuno-Dynamics' products. The most significant observation for each product is also indicated in summary form.

COMPARISON OF COMPETITOR PRODUCTS
(as a % of Immuno-Dynamics' product values)

Product	Total Protein	Fat	Lactose	IGF-1	Leptin	Insulin	Lactoferrin	Beta-Lactglobulin	Thymosin alpha-1	Thymosin beta-4	IgG	Summary of Observations
A	53.81	24.01	66.49	30.37	40.29	67.71	22.25	83.93	76.12	45.76	38.57	Colostrum collected 24+ hrs. after birth, fat removed
B	94.34	58.40	129.38	90.16	81.22	90.11	92.63	125.94	97.54	87.79	69.12	Colostrum collected late, some fat removed
C	99.16	59.24	289.57	49.83	169.19	342.76	36.27	120.84	64.05	91.03	36.23	Colostrum collected late; some fat removed
D	75.13	8.55	43.13	98.71	46.36	4.36	105.72	115.04	41.45	BDL	113.18	Colostrum collected late; fat and lactose removed
E	101.35	76.12	95.24	42.12	51.83	37.31	43.68	343.71	66.77	90.96	49.76	Colostrum collected late; some fat removed
F	92.49	62.76	120.40	75.14	72.51	66.55	97.73	67.86	81.92	88.35	78.64	Colostrum collected 6-8 hrs. after birth, some fat removed
G	134.62	5.52	87.15	36.87	45.80	28.87	50.67	109.84	81.55	105.20	54.12	Colostrum collected late; fat removed
H	99.60	23.83	89.85	108.08	117.87	102.69	52.26	88.89	78.46	87.93	44.21	Colostrum collected late; most of fat removed
I	132.82	5.26	97.04	53.65	101.94	144.80	67.34	155.29	101.53	96.53	47.61	Colostrum collected late; most of fat removed

BDL = Below Detectable Limits of the Assay