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# 4LIFE TRANSFER FACTOR TRI-FACTOR FORMULA (NANOFACTOR/TRANSFER FACTOR) – FULL PRESCRIBING INFORMATION

*4LIFE RESEARCH*

TOGETHER, BUILDING PEOPLE®

**DIETARY SUPPLEMENT**

4LIFE TRANSFER FACTOR ® TRI-FACTOR FORMULA®

4LIFE TRANSFER FACTOR® TRI-FACTOR® FORMULA

**PRODUCT DESCRIPTION**

4Life Transfer Factor Tri-Factor Formula combines proprietary transfer factors and NanoFactor®molecules extracted from bovine colostrum and chicken egg yolk sources. These molecules contain antigen information which educates, enhances, and helps maintain immune system balance.

**TECHNICAL DESCRIPTION**

Transfer factors are molecules that communicate antigenic immunological information intercellularly and from a donor to a recipient. They support immune function through cell-mediated immunity (CMI). Transfer factors, which carry antigen-specific information to which all tested immune cells respond, are produced by mononuclear cells and serve to support and improve immune-mediated pathways. Mammalian transfer factors, including those of humans, are small molecules between 3,500 and 10,000 daltons. (1; 2) Transfer factors are polypeptides that consist of 40 to 44 amino acids (3) and have a conserved region and a variable region. From a molecular biological standpoint, these two properties are analogous to antibodies; however transfer factors’ functions of cell-mediated immunity (CMI) and nonspecific immunological activity differ almost completely from the functions of antibodies. The molecules that have a molecular weight of less than 3,500 daltons modulate immune response but they do not transfer delayed-type hypersensitivity (DTH). (1)

4Life’s transfer factors are sourced from the ultrafiltration of colostrum and from chicken egg yolks. (4; 5) The molecules obtained from the spray-dried ultra-filtrate of bovine colostrum are of two classes: the transfer factors present in the ultra-filtrate of ≤10,000 daltons and the nanofraction molecules that are present in the nanofiltrate of ≤3,500 daltons.

Transfer factors were first discovered in 1949 by Dr. H. Sherwood Lawrence when he demonstrated that CMI could be transferred from one individual to another by way of low molecular weight extracts of white blood cells. Transfer factors could transfer DTH of a specific form from a skin test positive individual to a skin test negative individual who subsequent to the transfer would skin test positive for that antigen. (6) In a subsequent study in 1955, Lawrence demonstrated that DTH could be passed serially, first from a skin test positive individual to a test negative individual, who became test positive, then six months later from the second individual to another test negative individual who became test positive. (7) At the time, antibodies were the focus of immune research and little was known of the importance of DTH and of the involvement of T-cells in immune response. Transfer factors promote wellness via cell-mediated immunity. These compounds are components of colostrum, an infant’s first meal. They bridge the generational gap by passing cell-mediated immunity from mother to infant.

**BIOLOGICAL AND PHYSIOLOGICAL ACTION**

Transfer factors’ preparations contain more than 200 different moieties of polypeptide molecules with a molecular weight of <10,000 daltons; each moiety potentially has a great number of epitope variations. These antigen-specific factors are synthesized in monocytes and stored in the cytoplasm or on the cell membrane. A significant body of evidence indicates that the primary biological function of transfer factors is to recruit and specifically sensitize previously uncommitted lymphocytes. These sensitized T-lymphocytes initiate the events of cell-mediated immunity, thereby promoting immunity not only at the site of antigen challenge but also throughout the body. (8) The effect

of transfer factors on antigen-mediated immunity via B-cells is not completely understood; however, a clinical test has reported an increase in particular antibodies, such as IgA and IgG, during transfer factor administration.

Clinical studies have demonstrated that transfer factors’ unique ability to express DTH and promote cell-mediated immunity can be transferred from a sensitized donor to a non-immune recipient. (1; 9) This antigen-specific effect is well documented and is likely produced through activation of the CD3-antigen site of T-cells, increased macrophage activation, and interleukin production—which can also enhance natural killer cell function. (1; 10)

Although the exact mechanism of action is unknown, research has shown that transfer factors will bind to antigens. However, the antigen specificity that is “transferred” to recipients is mediated by T-lymphocytes. (3) Current structure function models propose that transfer factors have many, up to 818 possible, unique amino acids sequences, which allow transfer factors to be antigen specific (1). Transfer factors also have highly conserved regions that allow them to be administered across a species barrier without any loss of potency. In fact, research has demonstrated that bovine transfer factors are structurally analogous to human-derived transfer factors with equivalent physiological activity. (11) This is further supported by several studies, which used transfer factors extracted from bovine lymph nodes and colostrum to confer cell-mediated immunity to specific antigens in animals and human recipients. (12; 13)

Although most clinical trials with transfer factors have used parental administration, oral administration has also demonstrated successful transfer of DTH and cell-mediated immunity to recipients. (14) Dose response studies, which compare in various routes of administration, have been performed in both humans and animals. Results of these experiments refute any arguments that the acidic or enzymatic environment of gastrointestinal tract affects oral administration of transfer factors. (14)

#### CLINICAL AND EXPERIMENTAL STUDIES

##### *Natural Killer (NK) Cell Activity*

Peripheral blood mononuclear cells were isolated and pooled from several healthy donors. Sixty thousand cells were added to each well of 96-well microtiter plate. Various immune-modulating ingredients, including 4Life Transfer Factor® Tri-Factor® Formula, were added to select wells on the plate and the 48-hour incubation started. At end of the incubation period, 30,000 K562 cells were added to each well. MTT assay techniques were used to determine the cytotoxic index. The various 4Life Transfer Factor products resulted in cytotoxic indices of 80-98%. By comparison, mononuclear cells incubated with IL-2 for the same 48-hour period produced a cytotoxic index of 88%.

##### *CD4 T-Helper Cell Research*

Multiple studies were performed using the FDA-approved diagnostic CD4 T-Helper cell assay kit and/or a T-Cell Memory (CD8) assay kit under development by the same company. Similar to the NK cell research described above, these in vitro studies were performed on 96-well microtiter plates measuring ATP production via a luciferase-based luminescence reaction.

The CD4 assay utilized Phytohaemagglutinin (PHA)-stimulated cells isolated from whole blood via the use of Dynabeads™. An 18-hour incubation of these isolated, stimulated CD4 cells with 4Life Transfer Factor products resulted in a modulation of immune cell activity as exhibited by a decrease in Adenosine Triphosphate (ATP) production without a negative impact on cell viability. It is hypothesized that this reduction on ATP production is a result of a redirection in immune cell focus, essentially diminishing the distraction induced by the addition of PHA to the microtiter wells.

##### *Salivary Secretory IgA (SIgA)-Preliminary Investigation*

Twenty-four subjects na ve to transfer factor supplementation were enrolled in a small-scale, preliminary test. Twenty-one were included in the final analysis. Salivary samples were collected from each subject weekly at roughly the same time of day and day of the week. Saliva was collected over a 5-minute period via passive drool while subjects chewed on a piece of Parafilm™. The samples were put on ice and then frozen at -70°C until assay. The commercial Salimetrics™ salivary IgA assay kit was used for analysis. Subjects were given 4Life Transfer Factor® Tri-Factor®Formula at 2 capsules per day for two weeks and then transitioned to 4Life Transfer Factor®RioVida® Tri-Factor® Formula at 60 ml per day for an additional two weeks. At the end of the 4-week supplementation period, the group showed an average 73% increase in salivary secretory IgA (SIgA) production over their baseline value. Furthermore, none of the 21 subjects showed SIgA production rate less than their baseline value at the end of the test.

#### WELLNESS RESEARCH

A study conducted with 30 college students found that either l 15 days or 2 15 days (with a 2 weeks’ break in between) of transfer factor administered according to label dose helped them maintain their health. In both groups, transfer factor administration improved the number of CD8+ T-cells and NK cells to healthier levels. Particularly, those who took the product for 2 15 days showed prolonged health maintenance and improvement of immune cell markers than those who took it for 15 days. Specifically, the maintenance of good health

and improvement of immune cell markers remained for up to 3 months after stopping transfer factor administration in those who took the product for 2 15 days, in comparison to 1 month in those who took the product for 1× 15 days. (15)

**SAFETY**

In a study of acute toxicity, rats were assessed for 14 days following a single gavage of 4Life Transfer Factor. Five female SD rats were each gavaged with a dose of 2,000 mg/kg. No treatment-related mortalities occurred and there were no clinical signs of toxicity. No significant difference in body weight occurred. No gross lesions were found at necropsy in any of the animals. Thus, acute toxicity is considered to be greater than 2,000mg/kg (human equivalent dose of approximately 320 mg/kg). (16)

Another similar single-dose oral toxicity study was conducted in mice. Six female Wistar mice each received 2,000 mg/kg via oral gavage and monitored for 14 days. No observable toxicity occurred as assessed by mortality, body weight gain, histopathology of brain, liver, kidneys and lungs, clinical signs of aggression, lethargy, breathing difficulties, diarrhea, mobility, and shivering. Thus, the no-observed adverse effect level was considered to be greater than 2,006 mg/kg in mice, which is equivalent to approximately 9.7 g/day in humans. (17)

Recent toxicity studies performed by an independent toxicology laboratory were conducted to evaluate the mutagenicity and genotoxicity potential of 4Life Transfer Factor. Mutagenicity was assessed by the Bacterial Reverse Mutation assay. Results revealed that 4Life Transfer Factor has no mutagenic activity at any of the concentrations tested. Genotoxicity was assessed by the Mammalian Chromosome Aberration test. Results demonstrated that 4Life Transfer Factor, tested up to the maximum recommended concentration, did not induce structural chromosome aberrations in this mammalian system. The laboratory concluded that 4Life Transfer Factor is considered not clastogenic in this system.

Another recent study performed by the same toxicology laboratory assessed the oral toxicity of 4Life Transfer Factor in rats. In this 14-day repeated dose study, male and female Wistar rats received by oral gavage 1050, 2100, or 4200 mg/kg body weight/day of 4Life Transfer Factor or placebo. Results revealed that no mortality occurred at any given dose. Clinical observations showed no adverse effect of 4Life Transfer Factor on behavior and physical condition of the animals. No abnormal body weight gain of food consumption were observed. Ophthalmological and hematological evaluations demonstrated no adverse effect by 4Life Transfer Factor. Similarly, no changes were observed in clinical chemistry, gross pathology, organ weight, and histopathology at any given dose. It was concluded that the no-observed adverse effect level was greater than 4200mg/kg in rats. This dose is equivalent to 40g/day in humans (18).

The use of transfer factors is contraindicated in people receiving immunosuppressive therapy, though actual interactions have not been documented. The use of transfer factors during pregnancy and nursing has not been evaluated.

**HOW SUPPLIED**

- 4Life Transfer Factor® can be found in the following products:
- 4Life Transfer Factor® Tri-Factor® Formula
- 4Life® Transfer Factor Plus® Tri-Factor® Formula
- 4Life Transfer Factor® RioVida® Tri-Factor® Formula
- 4Life Transfer Factor® Chewable Tri-Factor® Formula
- 4Life Transfer Factor® Classic
- 4Life Transfer Factor® Immune Spray
- 4Life Transfer Factor® KBU®
- 4Life Transfer Factor® Belle Vie®
- 4Life Transfer Factor® Cardio
- 4Life Transfer Factor® GluCoach®
- 4Life Transfer Factor® MalePro®
- 4Life Transfer Factor® ReCall®
- 4Life Transfer Factor Reflexion®
- 4Life Transfer Factor Vista®
- Renuvo®
- RiteStart® Men
- RiteStart® Women
- RiteStart® Kids & Teens
- Pre/O Biotics™
- PRO-TF®

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## PRODUCT PHOTO

NOTE: These photos can be used only for identification by shape, color, and imprint. They do not depict actual or relative size.

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