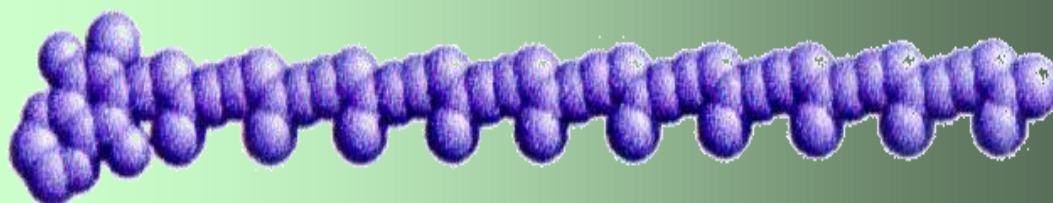


# BIO - COENZYME Q10



***COENZYME Q:  
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# INDEX

[Introduction](#)

[Structure and Function](#)

[Occurrence and Distribution](#)

[Bioenergetics and the Heart](#)

[CoQ and Cancer](#)

[CoQ and Muscular Dystrophies](#)

[CoQ and Diabetes](#)

[CoQ and Periodontal Disease](#)

[CoQ and Immune Function](#)

[CoQ and AIDS](#)

[CoQ and Peroxidation](#)

[CoQ and Brain Function](#)

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# INDEX

[Using Coenzyme Q10](#)

[Co-Enzyme Q10 and The Skin](#)

[Dissolution and Relative Bio-availability of Bio-Co-Enzyme Q10 purum](#)

[Bio-CO-ENZYME Q-10](#)

[Technical Specification](#)

[Material Safety Data Sheets](#)

[Metabolism of Cofactors and Vitamins; Ubiquinone biosynthesis](#)

[References](#)

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[best seller ingredient](#)
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[new innovations](#)
[contacting us](#)
[formularies](#)
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## ***Bio-Coenzyme Q10: Product Information Coenzyme Q: The Ubiquitous Quinone***

A.S. Gissen

### **Introduction**

#### **Part 1**

Coenzyme Q (CoQ), also known as ubiquinone, is a naturally-occurring substance classified as a fat-soluble quinone with characteristics that are common to vitamins. Its chemical structure is similar to that of vitamin K, and it is found naturally in the tissues of animals and plants. Coenzyme Q is one of the substances in the chain of reactions which produces energy in the metabolism of food. Because of the necessity of CoQ for energy production, almost every cell of a living organism contains CoQ. The CoQ content varies in different organs, being highest in those that produce large amounts of energy. In humans, CoQ is found in relatively high amounts in the heart, liver, kidney, and pancreas.(1) CoQ helps drive the mitochondrial energy production vital to all body functions. The functioning of all organs depends on each cell having adequate levels of CoQ to provide life-sustaining energy.

#### ***Structure and Function***

Coenzyme Q was first discovered in 1957 by Dr. Frederick Crane and his associates at the Enzyme Institute of the University of Wisconsin, when it was isolated from beef heart and shown to be essential in the process of bioenergetics.(2) A year later, Dr. Karl Folkers and his coworkers at Merck & Co., Inc., had succeeded in establishing its structure. The structure of the Coenzyme Q molecule is that of a quinone with an isoprenoid side-chain, the number of isoprene units in the side chain varies with each species of animal or plant. Humans contain Coenzyme Q10, which has 10 isoprene units.

Coenzyme Q is one of a family of brightly colored substances (quinones) that are widely distributed in nature because they are essential for generating energy in living things that use oxygen. The name ubiquinone was derived from the ubiquitous nature of these quinones. Coenzyme Q is a true coenzyme. A coenzyme is a substance that is necessary for, or enhances, the function of an enzyme. Bioenergy enzymes are necessary for a cell to generate energy from its food substances. The cell then uses this energy for its life processes. Coenzyme Q is an essential coenzyme for several of these bioenergy enzymes.

In cells, the process of generating energy takes place within the mitochondria, which are the energy-producing structures. In the mitochondria, molecules of coenzyme Q continually shuttle between bioenergy enzymes, transporting protons and electrons from one bioenergy enzyme to another. Cells in the body must continuously generate energy to support their function, and this process depends on each cell having adequate amounts of CoQ with which to generate this energy.

With such a fundamental role in energy production, it would be expected that deficiencies of CoQ would be detrimental to the bodies ability to function properly. Since CoQ is indispensably involved in the complex mechanism of respiration, including ATP formation, it is evident that a significant deficiency of CoQ in cellular respiration may have some detrimental effect upon the life processes dependent on energy, including mechanical, electrical, transport work, and biosynthesis. This deficiency could be reflected by one or more disease states, depending on the location and degree of the cellular deficiency of CoQ. Therefore, it is not surprising that CoQ deficiency has been linked to such diverse conditions as heart disease, heart failure, hypertension, muscular dystrophy, cancer, physical performance and athletics, diabetes, obesity, periodontal disease, aging, immune function, cellular antioxidant protection, and brain function.

## ***Occurrence and Distribution***

CoQ10 in the human body is thought to be provided not only by its biosynthesis in the body, but also from dietary intake of CoQ from food.(3) However, it is not clear how much exogenous CoQ contributes to maintain the body stores of CoQ10. Since CoQ is found in many foods, and is biosynthesized within the human body, the question of whether a dietary source of CoQ is essential has been considered. CoQ is found in almost all foodstuffs, albeit in small quantities. Wheat germ and rice bran are fair sources of CoQ, as is soy and some other beans. Vegetables are fairly low in CoQ, although spinach and broccoli are good sources. The major sources of CoQ in the human diet, however, are meats, fish, and vegetable oils. Soybean, sesame, and rapeseed oils are high in CoQ10, while corn oil is high in CoQ9. The average person consumes approximately 5 milligrams a day of CoQ, a level insufficient to obtain sufficient CoQ for their needs. The remainder of the CoQ10 needed by the body is synthesized in the cells, especially within the liver.

The production of CoQ10 in the body is a complex process. At least 15 different reactions are necessary (each catalyzed by an enzyme), as well as a number of cofactor substances including vitamins B3, B5, B6, B12, C, and folate.(4) In spite of its complex manufacture, most CoQ10 is made within the body. There is good evidence, however, that dietary CoQ contributes significantly to the endogenous body-pool of CoQ10. This has been shown in patients receiving total parenteral nutrition (TPN) that contains no CoQ. In these patients, who are dependent totally on endogenous CoQ10 synthesis, CoQ10 levels dropped by almost 50% within 1 week on a diet free of CoQ.(5) These levels remained depressed for the 12 weeks of the study. This represents good evidence that dietary sources are indeed a significant contributor to the body pool of CoQ10.

## ***Bioenergetics and the Heart***

The discovery of Coenzyme Q, as well as its function, structure, and ultimate synthesis, was made in America. The structure was elucidated, and CoQ10 was synthesized by Dr. Karl Folkers at Merck & Co. However, Merck & Co. decided not to pursue CoQ10 commercially. This gave the Japanese an opportunity to produce CoQ10 by synthesis in 1964, and ultimately, by fermentation in 1977. CoQ10 was clinically developed by the Eisai Co., Ltd., to treat congestive heart failure, and it was approved in 1974 by the Japanese government.

In 1977, a critique of CoQ10 in biochemical and biomedical research, and of ten years of clinical research with CoQ10 on cardiovascular disease, was published.(5) This paper was written to make known the clinical results published in Japan, from ten years of studying the administration of CoQ10 to cardiac patients. These 24 studies encompassed clinical data from 110 physicians in 41 medical institutions. The consensus from this decade of clinical research indicated a therapeutic benefit in about 75% of the patients having congestive heart failure. In addition, essential hypertension and angina pectoris appeared to have been improved by treatment with CoQ10. As a result of these studies, the Japanese government approved CoQ10 to treat congestive heart failure in 1974. By 1982, it was among the five most widely-used drugs in Japan. Despite a lack of interest in the US pharmaceutical industry, CoQ research began in earnest in the late 1970's with the availability of inexpensive, mass-produced CoQ10 from Japan. The vast majority of this research was conducted by independent researchers, as no US pharmaceutical company was interested in developing a non-patentable, natural compound like CoQ10, regardless of its potential.

In a 1985 review article, a total of 67 clinical studies involving some 1353 patients that had been treated for heart and blood vessel disease were presented. In these studies, CoQ10 was tested against heart muscle disease, arrhythmias, damage to the heart from drugs, high blood pressure, and stroke.(6) In those patients with heart muscle disease, approximately 75% showed meaningful clinical improvement. In fact, a study published in 1990 showed that CoQ10 significantly improved the survival of cardiomyopathy patients compared to treatment with traditional drugs.(7) After 3 years, 24% of the patients on conventional treatment were alive, while 75% of the CoQ10 patients were alive. In addition, most patients with mild cardiomyopathy

became normal on CoQ10 therapy. These studies also indicated that CoQ10 could successfully treat patients with arrhythmias, angina, ischaemic heart disease, stroke, and high blood pressure. In an animal model of cardiomyopathy, CoQ10 was found superior to digoxin, a traditional drug of choice, in attenuating disease progression.(8) Additionally, a recently published study showed that heart failure patients who were candidates for a heart transplant, and were instead treated with CoQ10, improved significantly.(9) All patients improved, with many requiring no conventional drugs and having no limitations on life-style.

Although CoQ10 has proven to be an effective treatment for congestive heart failure, two other nutrients have proven to be synergistic with CoQ10 in the treatment of congestive heart failure. These nutrients, carnitine and taurine, are similar to CoQ10 in being consumed in the diet, and produced by the body. Carnitine has been shown to be synergistic and complementary to CoQ in energetic metabolism, providing improvements in energy production that CoQ10 or carnitine alone are incapable of.(10) Taurine, on the other hand, resulted in improvements in congestive heart failure that were not observed in CoQ10 treated patients, although both groups improved.(11) These results with taurine are particularly interesting, as it has been known for some time that taurine deficiency in cats results in dilated cardiomyopathy, and cat food is now supplemented with taurine to prevent this affliction. There seems little doubt that in the case of heart failure, the utilization of CoQ10, carnitine, and taurine would be a useful and effective combination.

Beyond its well researched and approved (in Japan, Italy, Sweden, Denmark, and Canada) indication for congestive heart failure, CoQ10 is an important component in other aspects of cardiovascular health. To begin with, CoQ10 treatment reduces blood viscosity in patients with ischaemic heart disease.(12) This is something that more dangerous blood- thinning drugs are usually used for. Additionally, dietary supplementation with CoQ10 results in increased levels of CoQ10 within circulating lipoproteins, and increased resistance of human low-density lipoprotein (LDL) to the initiation of lipid peroxidation.(13) This may have far reaching implications for the development and progression of atherosclerosis, as oxidized LDL has been directly implicated in the pathogenesis of artery blockage and coronary artery disease.

The rationale for the use of CoQ10 treatment to provide protection for the heart in ischaemic cardiovascular syndromes was initially provided by animal studies which showed that CoQ10 pretreatment provided significant protection to the ischaemic myocardium (heart muscle).(14) Based on these positive results in animal studies, human clinical trials were initiated. A number of clinical trials using CoQ10 in chronic stable angina have been reported. The results of a double-blind study comparing oral CoQ10 to placebo showed that exercise time before distress was significantly increased in the CoQ10 treated group.(15) Another study showed that CoQ10 caused a significant reduction in cumulative exercise-induced electrocardiogram (ECG) abnormalities when compared to placebo.(16) In this study, CoQ10 also caused a reduction in exercise-induced systolic blood pressure from placebo values. It appears that CoQ10 treatment may allow ischaemic tissue to reach higher levels of energy expenditure before the onset of symptoms or exercise-induced ECG changes. The conclusion of these studies is that CoQ10 has a favorable effect on exercise tolerance with minimal adverse reactions.

One of the serious complications of cardiac surgery is the damage caused to the myocardium. During many cardiac surgical procedures the heart tissue is rendered ischaemic, due to lack of blood flow during surgery. Subsequently, the heart is reperfused when blood flow is resumed. It is during this reperfusion phase that much of the damage to the heart muscle takes place. The consequence of this damage is usually manifested by post-reperfusion arrhythmias and low cardiac output. It has been demonstrated that both damage secondary to reperfusion and post-reperfusion arrhythmias can be inhibited by pretreatment with CoQ10.(17) Because of its ability to protect myocardial tissue during ischaemic reperfusion, CoQ10 has been evaluated in patients undergoing cardiac surgery. CoQ10 pretreatment significantly reduced the incidence of low cardiac-output postoperatively.(18) CoQ10 has also been evaluated in patients undergoing coronary- artery bypass surgery. It was found that the CoQ10 treated group had significantly

higher cardiac output, lower requirements for post-surgical drug support, and significantly lower levels of creatine phosphokinase-MB (an indicator of heart tissue damage).(19)

Several different classes of pharmaceuticals have side-effects that include negative impacts on heart function. Some of these drugs, such as doxorubicin (a powerful anti-cancer drug) have cardiovascular effects so severe that they are strictly limited in their use by the extent to which the patients heart-function deteriorates while taking the drug. Others, like some psychotropics such as phenothiazine neuroleptics and tricyclic antidepressants, have a less severe effect on heart function; this cardiac side-effect, however, often makes their continued use dangerous or impossible. Even drugs such as beta-blockers, which are used to lower blood pressure and protect the cardiovascular system, have been shown to interfere with the production and function of CoQ10, and detrimentally effect heart function. In the case of doxorubicin, it was shown that the negative effects of this drug on heart function was due to its inhibitory effects on CoQ10-dependent enzyme systems.(20) Subsequent to this discovery, it was shown in cancer patients treated with doxorubicin that patients pretreated with CoQ10 had a reduction in doxorubicin's cardiotoxicity.(21) Interestingly, the use of CoQ10 with doxorubicin results in a two-fold increase of anti- tumor activity, in addition to CoQ10's ability to reduce side-effects.(22) In fact, this combination therapy may allow larger, and thus more effective, doses of doxorubicin to be administered before cardiotoxicity becomes a problem.

Undesirable cardiac effects have often been reported from the clinical use of phenothiazine neuroleptics and tricyclic antidepressants.(23) ECG abnormalities and arrhythmias appear to be the predominant cardiac abnormalities caused by these drugs, although heart failure and infarction are not uncommon. Furthermore, there have been increasing reports of sudden unexplained death with the administration of psychotropic drugs. CoQ10 reversed most effectively the inhibition of CoQ10-dependent enzymes caused by phenothiazines and most tricyclic antidepressants, and improved electrocardiographic changes in patients on psychotropic drugs.(23) One of the most commonly used classes of drugs in medicine are the beta-blockers. These drugs, used for the control of high blood pressure, are generally considered to be safe and effective. These drugs, however, are known to have antagonistic activities for CoQ10-dependent enzymes.(24) Since CoQ10 also lowers blood pressure in hypertensive patients, it would seem logical that the combination of beta-blockers with CoQ10 would be a particularly effective treatment, both for better control of blood pressure and the prevention of CoQ10 inhibition by the beta-blocker. In fact, this combined modality has been extensively reviewed, and found to be successful.(24)

Of all the drugs that have been found to lower the activity of CoQ10-dependent enzymes, none is more troubling than a class of drugs known as HMG-CoA reductase inhibitors. In recent years, these drugs have gained wide clinical acceptance as safe and effective treatments for elevated cholesterol. One of the more popular drugs in this category is known as lovastatin, although there are numerous others being developed as pharmaceuticals both in the US and abroad. These drugs work by inhibiting an enzyme known as HMG-CoA reductase, and they are very effective in lowering cholesterol levels. However, this enzyme is responsible not only for the production of cholesterol, but also for the production of CoQ10. Thus, the cholesterol lowering effect of these drugs is mirrored by an equivalent lowering of CoQ10. In patients with existing heart failure, lovastatin causes increased cardiac disease.(25) This deterioration was life-threatening for some patients. Interestingly, those patients given oral supplements of CoQ10 along with lovastatin had an improvement of cardiac function when compared to the patients given only lovastatin. There is evidence, however, that HMG-CoA reductase inhibitors cause morphological and physiological changes in cells that are not prevented by the replacement of CoQ10.(26) Indeed, the long-term effects of this class of drugs may indeed be very negative, keeping in mind the detrimental effects of lowering the body's CoQ10 levels. Not surprisingly, known side effects of these drugs include liver dysfunction and heart failure. Ironically, supplements of CoQ10 have been shown to lower cholesterol levels by feedback inhibition of HMG-CoA reductase.(27) Although the cholesterol lowering effect of CoQ10 awaits definitive proof in controlled studies, it may someday prove to be an interesting and healthful alternative to currently available cholesterol-lowering drugs.

## Part 2

In part 1 of our review on Bio-Coenzyme Q10, we examined the broad range of clinical and experimental evidence of CoQ10's vital role in the process of cardiac bioenergetics. Since its introduction into clinical research in the mid 1960's, most CoQ research has centered on its vital role in cardiac health. During the past thirty years, however, a large body of evidence has accumulated suggesting that the implications of CoQ deficiency go far beyond its well researched role in cardiac health. In this, part 2 of our examination of CoQ, we will discuss the far reaching implications of CoQ deficiency in conditions as varied as cancer, muscular dystrophies, physical performance and athletics, diabetes, and periodontal disease.

### *CoQ and Cancer*

Recently, a review of 15 years of experience with the administration of CoQ10 to cancer patients was published.(31) This paper examined eight new case histories, in addition to two earlier reported cases. The results of these cases supports the earlier findings that therapy of cancer patients with CoQ10, which has no significant side effect, allowed survival of these patients on an exploratory basis for periods of 5-15 years. All of these patients were receiving CoQ10 supplementation for heart failure, and CoQ10's anti-tumor effect was discovered by accident. These patients had cancers of the lung, pancreas, larynx, breast, and prostate. Unfortunately, interest in the use of CoQ10, either alone or as adjunct therapy in the treatment of cancer, has been lacking. This is surprising since many of the patients in these preliminary studies were considered to be terminal before beginning CoQ10 therapy. Indeed, the authors of this latest review called for systematic protocols to begin based on these extremely encouraging results.

### *CoQ and Muscular Dystrophies*

At present, several hypothesis suggest that muscular dystrophy results from some type of metabolic deficiency. This defect is manifested by an abnormality in muscle structure that gives rise to the death of the muscle fibers and to the abnormal muscle regeneration that is a characteristic of muscular dystrophy. As early as 1966 it was shown that in mice with genetic muscular dystrophy, CoQ administration would produce improvement.(28)

An interesting observation in humans was that virtually every form of muscular dystrophy is associated with cardiac disease.(29) This, coupled with early success using CoQ in animal models of muscular dystrophy, led to experimentation with CoQ10 administration in human forms of muscular dystrophy and neurogenic atrophies.

Muscular dystrophy is not a single disease, but rather, a group of closely related syndromes. The use of CoQ10 supplementation has been tried in a large number of these syndromes including the Duchenne, Becker, and limb-girdle dystrophies, myotonic dystrophy, Charcot-Marie Tooth disease, and Welander disease.(29) In these patients, improvements in physical well-being was commonly observed. Additionally, a direct relationship between muscle and cardiac impairment was found, as both of these improved on CoQ10 therapy. A later study, that also included some additional forms of muscular dystrophies (fascioscapulohumeral muscular diseases and hypotonia congenitale), also showed improvements in cardiac function for almost all patients, as well as improved physical performance and quality of life for many patients.(30) The authors concluded that therapy with CoQ10 is without any side effect, and may be given for the lifetime of the patients with muscular dystrophy. They also noted that there is presently no therapy for such patients which provides the improvement in quality of life as does CoQ10.

CoQ, Physical Performance, and Athletics With its central role in the production of energy, it is not surprising that the relationship between CoQ levels and physical performance has received considerable attention. The results of this research have shown that athletes, as opposed to sedentary individuals, have lower levels of serum CoQ10 and higher levels of muscle CoQ10.(32) Sedentary individuals showed the opposite pattern, with serum levels of CoQ10



being higher than muscle levels. Studies assessing the changes in CoQ10 levels with increasing physical activity have clearly shown that with an increase in exercise levels, CoQ10 levels increase substantially in both the heart and muscles.(33) This exercise-induced increase in CoQ10 levels has even been shown to prevent or reverse the age-related decline in muscle mitochondrial CoQ10.(34) Due to this relationship between muscle energy-output and CoQ10 levels, the administration of CoQ10 has been examined both in highly trained athletes, and sedentary individuals, for any positive effect on energy output and athletic performance.

In highly trained athletes, the administration of CoQ10 has been shown to increase both total energy output and time to exhaustion.(35) Of the parameters examined before and after exercise, several seemed to be affected by the administration of CoQ10. As in other studies, it was found that highly trained athletes had lower levels of serum CoQ10, and this level was significantly raised by CoQ10 administration. A comparison of serum markers of muscle damage showed a significant drop after supplementation of CoQ10, indicating that the use of CoQ10 resulted in a large decrease in the amount of muscle damage caused by exercise. In the case of sedentary individuals, CoQ has proven to be effective in increasing work output in normal, sedentary individuals,(36) as well as have a beneficial effect on impaired aerobic function in people complaining of fatigue with no medical origin.(37)

Other studies have shown that while short term CoQ10 supplementation has little effect on aerobic function in trained athletes, it does have significant effects on anaerobic function. This increase in anaerobic function led to increases in exercise duration, maximum oxygen consumption, maximum heart rate, and performance.(38) Interestingly, this study showed not only increases in cardiovascular and muscular efficiency, but also an increased tolerance to blood lactic acid levels. Based on the evidence that trained athletes have lower serum CoQ10 levels, it seems that supplementation may be necessary to ensure adequate levels of CoQ10 in the muscles, blood, and other organs.

### ***CoQ and Diabetes***

Although the investigation of CoQ10 levels in diabetics is relatively new, initial results have shown that deficiencies of Q10 may play a role in the pathogenesis of diabetic complications. The pancreas is an organ that contains large amounts of CoQ10,(39) and a deficiency of CoQ10 would be expected to impair the ability of the pancreas to produce adequate amounts of insulin. The activity of CoQ10-dependent mitochondrial enzymes in diabetic patients has been found to be significantly lower than that of controls.(40) It was concluded that this deficiency of CoQ10 may contribute to the development of diabetic complications, including cardiovascular disease and neuropathy. The blood levels of vitamin E were also found to be depressed in some of these patients, indicating that both bioenergetics and antioxidant capacity may be defective in diabetics. Three patients from the group with the most organ complications died from heart failure within a few months of CoQ10 measurement, and all of these patients had very low serum-CoQ10 levels, among the lowest in the study group, as well as low levels of serum vitamin E. In a supplementation study, the administration of CoQ10 to diabetic patients gave a reduction in fasting blood sugar levels in 36 percent of the cases, and a reduction in blood ketone bodies in more than half the cases.(41) These results in both insulin and non-insulin dependent diabetics, although preliminary, are certainly encouraging. Due to the serious nature of diabetic organ-complications, the rationale for the use of CoQ10 is certainly strong. In fact, the combined use of CoQ10 and vitamin E, based on these findings, may represent a useful combination for the control and/or prevention of diabetic complications.

### ***CoQ and Periodontal Disease***

Periodontitis is a very common disease in all parts of the world. The main cause of the disease is deposition of plaque on the teeth and the inhabitation of bacteria in the area between the gingiva and the teeth. Both oral hygiene and nutritional status have been shown to affect the condition of periodontal tissue.(42) However, periodontal disease often affects persons without any obvious reason, especially with advancing age. Early research examining healthy and

diseased gingiva showed a significant deficiency of CoQ10 in diseased gingiva, but not in healthy gingiva.(43) In light of this apparent deficiency of CoQ10, trials were conducted to determine the effects of CoQ10 supplementation on the progression of periodontal disease.

The oral administration of CoQ10 to patients with periodontal disease was effective in reducing gingival inflammation, as well as periodontal pocket-depth and tooth mobility.(43) Not only did these improvements not occur in the placebo group, but the researchers correctly assigned what patients received CoQ10 or placebo in every case. Because periodontal disease is often resistant to treatment with improved hygiene or surgical intervention, CoQ10 supplementation may represent an important step in improving periodontal health.

### **Part 3**

In part 2 of our review of Coenzyme Q10 (CoQ10), we examined the broad spectrum of research into CoQ's role in varied conditions such as cancer, muscular dystrophies, physical performance and athletics, diabetes, and periodontal disease. In the third and final part of our look at CoQ, we will explore the role that CoQ10 plays in immune function, antioxidant protection, and brain function.

### ***CoQ and Immune Function***

Vitamin and nutritional deficiencies are well known to be common causes of immunodeficiencies. Persons having nutritional and vitamin deficiencies have impaired cell-mediated immunity, as well as decreased microbicidal activity of immune cells and increased susceptibility to infections. Being vitally important to the generation of cellular energy, it is not surprising that deficiencies of CoQ result in suppression of the immune system. However, the result of supplemental CoQ10 is quite provocative, as it produces a significant enhancement of the immune system in both normal and immuno-depressed animals.

In 1970, it was first reported that CoQ6 and CoQ10, when administered to rats, significantly enhanced the activity of immune cells' ability to kill bacteria, as well as elevating their antibody response.(44) By 1982, more than half a dozen studies had documented significant immunological enhancement following the administration of CoQ10. These results included decreasing the number of tumors, and increasing the number of survivors, following exposure to carcinogens;(45) increasing the number of survivors following exposure of rats to a leukemia-inducing virus, which interestingly caused a CoQ deficiency after infection;(46) and reversing an age-related decrease in CoQ levels in the thymus of aging animals.(47) The immune potentiating activity of CoQ was paralleled by a protection of immune-suppressed animals against otherwise lethal infections.(48) When compared to other antioxidants like vitamin E, it was found that these immune-enhancing properties were specific to CoQ, as the antioxidants did not stimulate the immune system to an equal degree.(49) A similar activity of CoQ10 was also found in human patients with conditions such as diabetes, cancer, and cardiovascular disease, with CoQ10 administration resulting in significantly enhanced levels of immunoglobulins (IgG).(50)

At a 1981 conference on Coenzyme Q, several reviews were presented that documented the significant role that CoQ has on immune function.(51) The conclusions of these researchers were that:

1. In extensive studies, using many experimental models which evaluated various parameters of immune function (phagocytic rate, antibody level, cancer, viral, and parasitic infections), a role of CoQ as an immuno-modulating agent was established.
2. During some infections and aging, an organism develops a Coenzyme Q- enzyme deficiency.
3. Results indicate that CoQ is an important component, probably at the mitochondrial level, for the optimal function of the immune system.

4. The lack of toxicity, as demonstrated in clinical and experimental tests, indicates that CoQ10 is an appropriate candidate for clinical application in disease states where the immune system is not functioning at an optimal level.

5. Research indicates that tumors, infections, and some of the immunity-related "diseases of aging" should be included in a new entity, "diseases of bioenergetics."

### ***CoQ and AIDS***

While the above results are certainly provocative, the most exciting immune-related research on CoQ10 has been in the area of Acquired Immune Deficiency Syndrome (AIDS). In the early 1990's, a series of reports were published showing that CoQ10 deficiency could play a role in the development of AIDS. These investigations were begun after the observation that, among other things, many AIDS patients have significant heart- function failure, similar to persons with CoQ10-deficiency related heart-failure.(52) Subsequent measurements of blood CoQ10 levels revealed that Human Immunodeficiency Virus (HIV) positive patients that were asymptomatic had normal levels of CoQ10, Aids Related Complex (ARC) patients had significantly lower levels, and full-blown AIDS patients had the lowest levels. Thus, AIDS was associated with CoQ10 levels that were severely and significantly depressed, while HIV-positive persons without symptoms had normal levels that declined as they progressed to ARC, and further declined as they developed AIDS. Based on these investigations, a small pilot-study was begun to investigate the effects of CoQ10 supplementation on patients with ARC and AIDS. The results of this study showed that ARC patients on CoQ10 therapy remained free of opportunistic infections and didn't progress to AIDS over a period of more than 4 years. The authors concluded that this excellent clinical response was possibly because, "... the delicate equilibrium between host and virus has been tipped in favor of the host in this disease state through the use of oral CoQ10."(52)

### ***CoQ and Peroxidation***

Free-radical mediated lipid-peroxidation appears to be of critical importance in various degenerative diseases, including atherosclerosis. Studies have suggested that the oxidative modification of low-density lipoprotein (LDL) is central to the induction of atherosclerotic changes in blood vessels. In research comparing the relative effectiveness of various antioxidants in preventing free-radical induced peroxidation of LDL, CoQ10 was found to be more effective than either lycopene (a carotenoid), beta-carotene, or vitamin E.(53) This effect was specific to the reduced form of CoQ10 (ubiquinol), and not oxidized CoQ10 (ubiquinone). Although oxidized CoQ10 (ubiquinone) is the only supplemental form of CoQ10, other studies have shown that dietary supplementation with CoQ10 results in increased levels of reduced CoQ10 (ubiquinol) within circulating lipoproteins, as well as increased resistance of LDL to the initiation of lipid peroxidation.(54) It appears that after oral supplementation, CoQ10 appears mainly in its reduced, antioxidant form in the body. Not surprisingly, research has shown that the ratio LDL to CoQ10 is an important indicator of the risk of developing atherosclerosis, being even more important than the often cited ratio of HDL to total cholesterol.(55) Indeed, while CoQ10 has been repeatedly shown to be a physiologically important lipid-soluble antioxidant, it may be the most important lipid-soluble antioxidant.

### ***CoQ and Brain Function***

It is well established that deficiencies of myocardial CoQ10 results in derangements of cardiac energy production, eventually leading to cardiac cell death. This is the biochemical basis for the success in using CoQ10 in cardiomyopathy. Recent evidence now shows that a similar mechanism may be involved in degenerative brain disorders. In the case of Parkinson's disease, research has shown that deficiencies in CoQ10-dependant enzymes may play a part in the development of the cell death that results in Parkinson's disease.(56) In Alzheimer's disease, as well, deficiencies of CoQ10-dependent enzymes have been found.(57) Attempts to improve the mental functions in Alzheimer's patients have been very encouraging, with reversals of mental deterioration being documented in several studies, including those using genetically-confirmed

Alzheimer's patients.(58) Although these preliminary studies await confirmation, it is not surprising that CoQ10 deficiencies, leading to cellular energy deficiencies, would result in the cell death that is a hallmark of both Parkinson's and Alzheimer's disease. In fact, the use of supplemental CoQ10 to prevent brain deterioration has been an indicated use of CoQ10 for many years in Japan.(59)

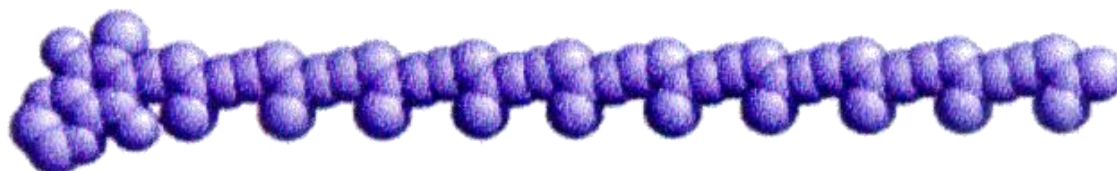
### ***Using Coenzyme Q10***

With the vast amount of positive results that have been published about CoQ10 in the last three decades, it is not surprising that CoQ10 has become one of the best-selling supplements in the United States. Few dietary supplements are as well proven, or hold as much potential for improving health, as does CoQ10. However, as with any biologically- active dietary supplement, how CoQ10 is used is important in order to attain maximum benefit from supplementation.

CoQ10 is fat-soluble, and like most other fat-soluble compounds, is poorly absorbed from the gastrointestinal tract, especially when taken on an empty stomach. For this reason it is important to take CoQ10 with meals to ensure maximum absorption. The dosage of CoQ10 is also a very important consideration. Although small dosages of CoQ10 will ensure a good dietary amount of CoQ, and prevent the decrease in blood levels seen when purified diets free of CoQ are consumed, they will not significantly raise blood levels in persons with depressed CoQ10 levels due to disease or aging. Human research has found that doses of at least 30 milligrams are needed to significantly raise blood levels of CoQ10.(60) Due to the vast amount of research that has been conducted on CoQ10 supplementation, dosages have varied over a wide range. In most of these studies CoQ10 was administered in two or three divided doses, with meals, throughout the day. The usual dosages used to correct CoQ10 deficiency in disease states has been from 60 to 200 milligrams a day. Also, the increase in blood levels seen after supplementation is not uniform, as some people seem to absorb CoQ10 poorly and require larger doses to attain maximum benefit. One important consideration to keep in mind when determining the appropriate dosage is that despite rarely occurring nausea or gastrointestinal upset, toxicity and side-effects have not been encountered in several decades of clinical use at doses up to several hundred milligrams a day. Younger persons, as well as persons with no CoQ10- related deficiency disease, may wish to supplement with CoQ10 in doses of 10-30 milligrams in one daily dose, or even consider taking 30 milligrams with one meal every other day. CoQ10 is fat-soluble, and has a half-life in the body of several days, so healthy persons can benefit from less frequent supplementation than those who have CoQ10-related diseases, and should take CoQ10 in several doses throughout the day.

When purchasing CoQ10, the purity of the material should be carefully considered. Very few companies in the world manufacture CoQ10, and the pharmaceutical-grade product in its pure state is a pure white to buff white color. CoQ10 has a very long shelf-life when protected from light and excessive heat, with little deterioration occurring over periods of up to several years at room temperature. When exposed to light, however, CoQ10 will degrade quite rapidly. If a CoQ10 product is being sold at a price that seems too good to be true, it probably is. Production of CoQ10 can barely meet the world-wide demand. Prices are relatively uniform between the different primary manufacturers. and should be among the different retailers.

### ***Co-Enzyme Q10 and The Skin***



Human Bio-Coenzyme Q10 with isoprenoid side chain consist of 10 isoprene units. Currently, CoenzymeQ10 is used for most of the Skin-Whitening cosmetics as it has been reported that the most of these whitening actives are involved in :

**"Total and complete inhibition of the amino acid Tyrosine and its formation**

*An important point should be noted here on Bio-CoEnzyme Q10 - an Essential Biomolecule that is present in all mammalian tissues; and any lackings in the levels of CoEnzyme Q10 presence and manufacture is related with myriads of physiological dysfunctions like the enhanced Aging processes. The formation of CoEnzymes Q10's quinone ring is synthesized from the Amino Acids Tyrosine and Phenylalanine(map 0130)*

*Total and complete inhibition of the amino acid Tyrosine and its formation as experienced with most of the presently available Skin Whitening Agents can be implicated in skin Aging and other complications. "*

*(Balasubramaniam M PhD 1995)*

*In cosmetic cremes and lotions, Bio-CoenzymeQ10 is an revolutionary anti-aging ingredient that restructures and stimulates the aging skin cells, and acts as a powerful anti-oxidant which tones and smoothen. The Bio-CoEnzyme Q10 maintains skin's energy andnaturally repairs cellular oxygen (radical oxygen) damage as an anti-oxidant.*

*The most famous introduction in cosmetic products is*

***Nivea Visage Anti-Wrinkle Cream Q10**, manufactured in Italy (mid way between Bergamo and Milan) and scheduled for launch in USA in October 1998.*

### Literature References:

Ernster, L. and Daliner, G (1995) Biochemical, Physiological and Medical Aspects of Ubiquinone Function. *Biochimica et Biophysica Acta*, 1271, 195-204.

(More literature references available on request for Skin-whitening Actives related non-positive skin lesions and blotch patches due to loss of CoEnzymes Q10 and related Skin Ceramides)

The following book offers a good general review of CoQ research for the layperson:

E. Bliznakov, **Coenzyme Q: The Miracle Nutrient**. Bantam Books, NY. 1986.

**The following six volume set offers a good review of CoQ research for the cosmetic scientist:**

K. Folkers, et al.(eds): *Biomedical and Clinical Aspects of Coenzyme Q*, Vol 1-6, Elsevier Science Publishers, Amsterdam. 1976 - 1991.

### Dissolution and Relative Bio-availability of Bio-Co-Enzyme Q10 purum

-----  
Abstract:

Currently available Coenzyme Q10 dosage forms exhibit negligible dissolution indicating potentially poor bioavailability. In order to improve its dissolution profile and thereby its absorption.

A new process was employed to produce Bio-Coenzyme Q10 purum . This novel isolate in the form of a waxy crystalline powder or soft mass is encoupled with the respective enzymes **EC:1.6.5.3** and made suitable for soft gelatin capsule (encapsulation) which can passed the USP Dissolution requirement for nutritional supplements. When compared with other commercially available dosage forms for relative bioavailability in human subjects, Bio-Coenzyme Q10 purum was found to be vastly superior (a 6 fold increase in plasma CoQ10 values over baseline, and up to 300% greater relative bioavailability over other dosage forms tested).

Coenzyme Q10 (Ubiquinone) is a lipid-soluble compound found in the mitochondria of all living cells. It also occurs in the food chain and is endogenously produced in the liver. There are conditions in which adequate production of CoQ10 in the body is impaired, and in such situations supplementation with CoQ10 has been shown to be very beneficial.

CoQ10, being lipid soluble, follows the same pathway as that of fats for its absorption in the body. This involves emulsification in the intestine (with the help of bile salts and various lipolyases) and the formation of micelles prior to absorption. Among the other factors affecting the absorption of exogenously administered CoQ10 are its particle size, degree of solubilization, and the type of food ingested with the supplement.

Although CoQ10 is classified as a lipid soluble substance, its degree of solubility is extremely limited. Commercially available CoQ10 capsules contain either oil-based suspensions (softgels), or dry powder with silicon dioxide and talc blends (hard gels). When tested in the laboratory, these products show a total lack of dissolution according to current USP methodology. Such lack of dissolution properties are often indicative of poor absorption and bioavailability.

In order to improve the dissolution profile and bioavailability of CoQ10, KAMPOYAKI RESEARCH SDN BHD (Malaysia) has acquired an exclusive technology (formulation/process) from BioTakenaka Pharm.Co, Japan. This novel Bio- Coenzyme Q10 purum process has provided the key to the solubilization of CoQ10. Bio-Coenzyme Q10 purumsoftsules® based on the Bio-

Coenzyme Q10 purum formulation and process exhibit complete dissolution, which is indicative of improved absorption/bioavailability.

A human study was subsequently carried out to compare the relative bioavailability of Coenzyme Q10 purum softgels with other currently available dosage forms (softgels, tablets and capsules), and the data obtained from the study clearly demonstrate that Coenzyme Q10 purum softgel is vastly superior (about 300% higher relative bioavailability than all other dosage forms tested).

These data are private and unpublished and are subjected to patent pending applications April 9, 1998.

(A new Coenzyme Q10 preparation with enhanced relative Bioavailability).

**Bio-CO-ENZYME Q-10 (coupled with enzymes) (ubiquinone)**

**DESCRIPTION**

Appearance : Waxy Hard Granules  
 Particle Size : Granules  
 Color : Buff Creamy Yellow  
 Aroma : Neutral  
 Taste : Characteristic

**Recognition Test**

Maximum absorbance of the oxidized solution is seen at 275+/-nm, and that of reduce solution at 290+/- nm.

Storage : Cool,dry area; Decomposes at around 48C (118F).

Comments **Bio-CoEnzyme Q10 Orange (Liquid Grade) for Cosmetic Formulations available**

**Analysis**

Assay (Ubiquinone) : NLT 99.5%  
 Co-Q9 (Ubiquinone homolog &enzyme\*) : NMT 0.2%  
 Moisture : NMT 0.2%  
 Ash : NMT 0.1%  
 Heavy Metals : NMT 20 ppm  
 Arsenic : NMT 2 ppm

**Microbial:**

E. Coli Negative  
 Salmonella Negative  
 Germs <100 cfu/gm Non-pathogenic  
 Yeasts/Molds < 100 cfu/gm

Enzyme coupling:

NAME: NADH dehydrogenase (ubiquinone) flavoprotein 2 (24kD) H.sapiens [EC:1.6.5.3]

CLASS Metabolism; Energy Metabolism; Oxidative phosphorylation [MAP:00190]  
 Metabolism; Metabolism of Cofactors and Vitamins; Ubiquinone biosynthesis [MAP:00130]

***This information is presented in the belief that it is accurate and reliable; however, no warranty, either expressed or implied and no freedom from liability form patents, trademarks, or other limitations should be inferred. Any data listed are averages only and are not to be considered as guarantees expressed or implied, nor as a condition of sale.***

**CAMPO RESEARCH Pte Ltd**  
**TECHNICAL SPECIFICATION**

<b>PRODUCT Name (Campo Research)</b>	<b>CAMPO BIO-CO-ENZYMES Q-10</b>
<b>Other Trade Names (Campo Research)</b>	UBIQUINONE Q10; COUPLED WITH ENZYMES CAMPO BIO-CO-ENZYMES Q-10
<b>Existing CTFA/INCI Name</b>	UBIQUINONE
<b>Chinese Translation</b>	泛醌 (UBIQUINONE)
<b>CAMPO PRODUCT #</b>	<b>98-2915 (WAX)</b>
<b>HS Code:</b>	1302.19.0000
<b>CTFA Monograph ID:</b>	10169 - UBIQUINONE
CAS#	303-98-0 / 60684-33-5 – Ubiquinone
CAS# EU	303-98-0 / 1339-63-5 / 60684-33-5 (EU) – Ubiquinone
EINECS Number and Name	206-147-9(1) – Ubiquinone
EINECS# EU	206-147-9 / 215-668-0 (EU) – Ubiquinone
EINECS Number and Name	Ubiquinone
EINECS# EU	<a href="http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details_v2&amp;id=38807">http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details_v2&amp;id=38807</a>
European Commission–Health & Consumer Cosmetics–Cosing	Ubiquinone – 206-147-9 / 215-668-0 (EU)
<b>BATCH/LOT</b>	<b>See COA Batch Lot</b>
<b>SPECIES</b>	-
<b>PARTS USED</b>	-
<b>RAW MATERIAL - ORIGIN</b>	Japan
<b>CONCENTRATION</b>	-
<b>COMMENTS</b>	A Quality Management System, compliant to the International Standard ISO 9001, was used to manufacture and test this material  <b>*Please take note that all specifications are liable to changes without prior notice.</b>

<b>Specification Parameter Analysis</b>	<b>Specification Range</b>	<b>Results</b>	<b>Methods</b>
Physical Form	Waxy hardened granules	Conforms	Visual
Color	Yellow amber waxy hardened granules	Conforms	Visual
Odor	Characteristic	Conforms	Olfactory
Aroma	Neutral	Conform	Olfactory
<b>Microbial:</b>			
E.Coli	Negative	-	-
Salmonella	Negative	-	-
Specific Gravity (20°C)	0.688 - 0.695	See COA	USP XXIX/Par, DMA35
Refractive Index (20°C)	-	-	USP XXIX/DGF IV C (52)
pH(20deg.C.) (100% Concentrate)	N/A	-	USP XXIX/DGF H III (92)
Water solubility	6-9%	Conforms	
Assay: Ubiquinone	NLT 99.5%	-	-
Co-Q9 (Ubiquinone Homolog & Enzymes)	NMT 0.2%	-	-
Saponification Value BS684 (4 hours)	15.00 - 24.00	See COA	
Acid Value BS684	0.000 - 2.00	See COA	
Iodine Value	4.000 - 8.0000	See COA	
Moisture	NMT 0.2%	-	-
Ash	0.000 - 0.250	See COA	G02301



Arsenic	NMT 2 PPM	-	-
Dry Residue (160deg.C/2hrs)	50.0 - 55.0	See COA	Mettler 16J
Preservation	None	Conforms	-
Pesticide Content	None	Conforms	Pflanzaniaschuttal 1989
Total Germs	<10 CFU/ml - non-pathogenic	Conforms	USP XXIX/Ph.Eur.2.6.12(97)
Total Yeast/Mold	Nil	Conforms	USP XXIX/Ph.Eur.2.6.12(97)
Heavy Metals(Total)As,Pb,Hg	NMT 20ppm	Conforms	USP XXIX/Ph.Eur.2.6.12(97)

CAMPO RESEARCH Pte. Ltd, SINGAPORE  
 CAMPO RESEARCH USA, INC SAN DEIGO CA 92111, & Manhattan, New York City, USA  
 CAMPO RESEARCH s.r.o., Brno, Czech Republic  
 CAMPO RESEARCH Pvt. Ltd, CHENNAI , INDIA  
 CAMPO RESEARCH CANADA LTD, TORONTO, CANADA

MATERIAL SAFETY & CONSUMER SAFETY TESTING LABS.  
 DIV. OF JTC KAMPOYAKI SINGAPORE  
EMERGENCY MATERIAL SAFETY / ACCIDENTAL RELEASE CENTER Contact:  
*Emergency Tel.no: +(65)-63833202/63833631(24hours) /63228551/63228503*  
*Emergency Fax No: +(65)-63833632(24hours),63824680, 63228558*  
*EMAIL: msds911@campo-research.com*

**Campo Bio-Co-Enzymes Q-10 ©.**

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**“(SAFETY DATA SHEET – compliant to GHS)”  
CONFIRMS TO EC DIRECTIVE 91/155/EEC, EC REGULATION  
NO#1272/2008, AMENDED EC REGULATION NO#790/2009 and  
Complies to The EU Cosmetic Products Regulation (Regulation (EC) No  
1223/2009) effective on July 2013., and to EU Commission Regulation  
No.358/2014/9 of 9<sup>th</sup> April 2014 amending Annexes II and V, to EU  
Regulation No No.1223/2009 of The European Parliament and of The  
Council on Cosmetic products, (Effective Date 31<sup>st</sup> October 2014) AND to  
US DEPT.OF LABOR-Occupational Safety & Health Admin directives and  
compliant to Globally Harmonized System of Classification and Labeling of  
Chemicals (hereinafter referred to as “the GHS”)., and Complies and  
Confirms to the Requirements of State of California Proposition 65.**

A Quality Management System, compliant to the International Standard ISO 9001, was used to manufacture and test this material

<http://www.osha.gov/dsg/hazcom/ghs.html>

[http://www.unece.org/trans/danger/publi/ghs/ghs\\_welcome\\_e.html](http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html)

<http://www.hc-sc.gc.ca/ahc-asc/intactiv/ghs-sgh/index-eng.php>

DATE OF FIRST ISSUE	February 10th 1992-Reviewer - Dr Balasubramaniam PhD
DATE OF LATEST REVISION	Dec. 10th 1996- Rev'wer- Dr Fergus Jes .G.Velasquez Bsc. Med Tech, MD <b>February 10<sup>th</sup> 2012 – Reviewer=Joshua Teo</b> <b>February 5<sup>th</sup> 2013 – Reviewer –</b> <b>Dr Balasubramaniam M, PhD</b> <b>12<sup>th</sup> February 2015 - Joshua Teo BSc. Chem,</b> <b>Balasubramaniam M PhD &amp; Oksana Nemchenko</b> <b>MD</b> <b>15<sup>th</sup> May 2016 - Joshua Teo BSc. Chem,</b> <b>Balasubramaniam M PhD &amp; Oksana Nemchenko</b> <b>MD</b>
<b>1</b>	<b>PRODUCT AND COMPANY IDENTIFICATION</b>
COMMERCIAL NAME:	<b>CAMPO BIO-CO-ENZYMES Q-10</b>
OTHER TRADE NAME:	<i>UBIQUINONE Q10; COUPLED WITH ENZYMES</i>
LATIN NAME:	-
CTFA ADOPTED NAME INCI NAME:	UBIQUINONE / CO-ENZYMES Q-10
Chinese Translation	泛醌 (UBIQUINONE)
<b>INTERNATIONAL CHEMICAL IDENTIFICATION</b> <i>(EC REGULATION NO#1272/2008 AMENDED NO#790/2009)and Compliant to the GHS:</i>	<b>UBIQUINONE / CO-ENZYMES Q-10</b>
EPA (USA) GENERIC NAME:	-
MANUFACTURER: (cGMP MFG. FACILITIES) :	<b>Campo Research Pte Ltd,</b> <b>Level 30, 6 Battery Road</b> <b>Singapore 049909</b>

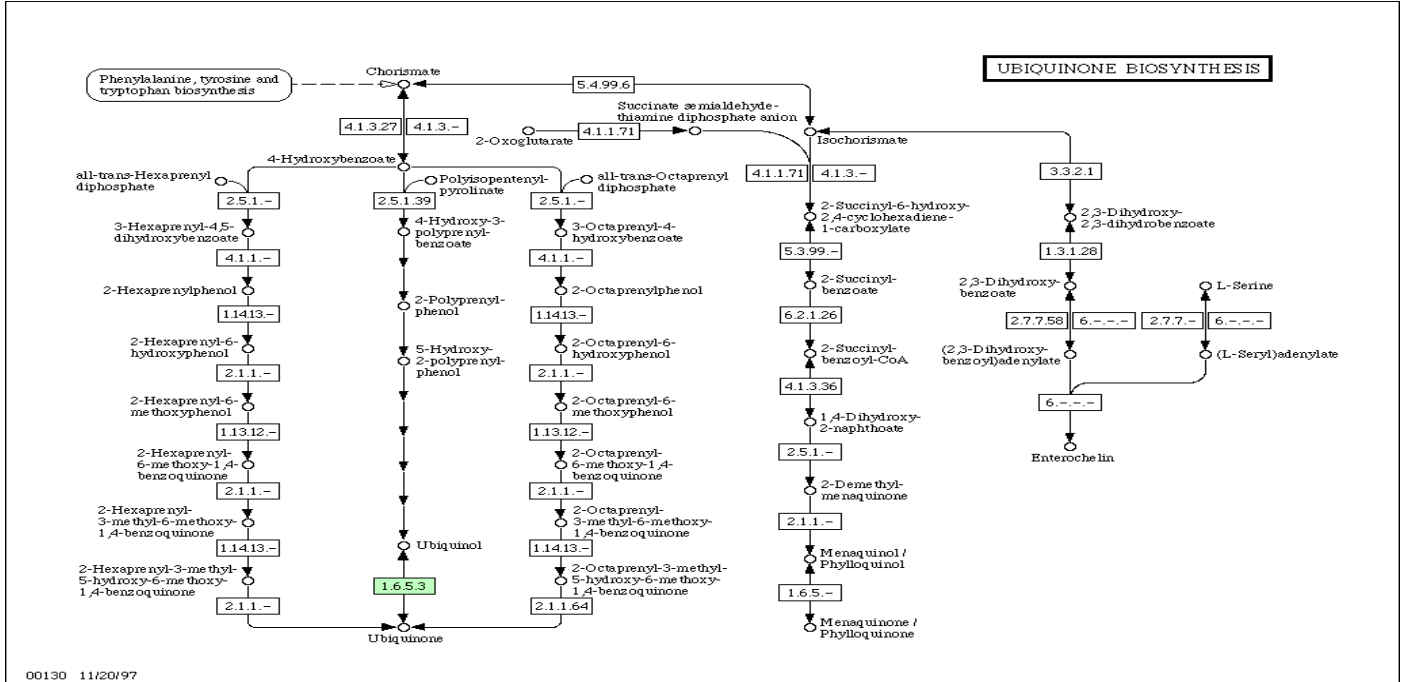
	EMERGENCY TELEPHONE NUMBERS:	<b>(65)-63833203/(65)-62837781 (Singapore)</b>
<b>2</b>	<b>HAZARDS IDENTIFICATION</b>	
	NOT CLASSIFIED AS DANGEROUS ACCORDING TO DIRECTIVE 67/548/EEC OR ITS AMENDMENTS.	DIVISION 1.6; NON-HAZARDOUS NO HAZARD STATEMENT
	<b>HAZARD CLASS and CATEGORY CODE(s)</b>	PICTOGRAM : NONE
	<b>HAZARD STATEMENT CODE(s)</b> <i>(EC REGULATION NO#1272/2008 AMENDED NO#790/2009) and compliant to the GHS</i>	No GHS Pictogram (Totally Non-Hazardous) Division 1.6; NO HAZARD STATEMENT
	<b><u>GHS CLASSIFICATION :</u></b> This material is Non-hazardous according To UN-GHS Criteria.	PICTOGRAM : NONE No GHS Pictogram (Totally Non-Hazardous) Division 1.6: No Hazard Statement.
	<b><u>GHS LABEL ELEMENTS:</u></b>	No GHS Pictogram (Totally Non-Hazardous) Division 1.6: No Hazard Statement.
<b>3</b>	<b>COMPOSITION / INFORMATION ON INGREDIENTS</b>	
	100 PERCENT CARBON DIOXIDE GAS EXTRACTED NATURAL VEGETAL COMPONENTS EXTRACTED IN WATER CARRIER MENSTRUM & FREEZE DRIED	<b>UBIQUINONE / CO-ENZYMES Q-10</b>
	CTFA Monograph ID:	10169 - UBIQUINONE
	CAS# CAS# EU	303-98-0 / 60684-33-5 – Ubiquinone 303-98-0 / 1339-63-5 / 60684-33-5 (EU) – Ubiquinone
	<b>CAS NO# (CAS Name)</b> <i>(EC REGULATION NO#1272/2008 AMENDED NO#790/2009)and compliant to the GHS</i>	<b>303-98-0 / 1339-63-5 / 60684-33-5 – Ubiquinone</b>
	EINECS Name and Number EINECS# EU	206-147-9 / 215-668-0 (EU) – Ubiquinone
	<b>EINECS# (EINECS Name)</b> <i>(EC REGULATION NO#1272/2008 AMENDED NO#790/2009) and compliant to the GHS</i>	<b>206-147-9 / 215-668-0 – Ubiquinone</b>
	EINECS Name and Number EINECS# EU European Commission–Health & Consumer Cosmetics–Cosing	Ubiquinone <a href="http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details_v2&amp;id=38807">http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details_v2&amp;id=38807</a> Ubiquinone – 206-147-9 / 215-668-0 (EU)
	RISK PHRASES SAFETY PHRASES 25-26	None Not Mandatory
	<b><u>GHS CLASSIFICATION :</u></b> This material is Non-hazardous according To UN-GHS Criteria.	<b>PICTOGRAM : NONE</b>
	<b><u>GHS LABEL ELEMENTS:</u></b>	<b>No GHS Pictogram (Totally Non-Hazardous Division 1.6: No Hazard Statement.</b>
<b>4</b>	<b>FIRST AID MEASURES</b>	
	EYE CONTACT:	Wash with water or standard eye wash solution. Seek medical advice, if irritation occur and persist.
	ORAL INGESTATION:	Edible in small quantity (10 gms) without adverse effects.

	SKIN CONTACT:	Wash with water or shower.
<b>5</b>	<b>FIRE FIGHTING MEASURERS</b>	
	<b>NON-COMBUSTIBLE AND PRESENTS NO SPECIAL FIRE HAZARD</b>	
	EXTINGUISHING MEDIA:	Treat as oil fire when store in HDPE drums with CO <sub>2</sub> , dry foam or dry chemical.
	PROTECTIVE EQUIPMENTS FOR FIGHTERS:	Standard Equipments.
<b>6</b>	<b>ACCIDENTAL RELEASE MEASURES</b>	
	ABSORB ONTO AN INERT MATERIAL AND SCRAPE UP. REMOVE RESIDUE BY SCRUBBING WITH HOT WATER OR DETERGENT SOLUTION.	
<b>7</b>	<b>HANDLING AND STORAGE</b>	
	STORE IN SEALED CONTAINERS UNDER NORMAL COOL, DRY WAREHOUSING CONDITIONS.	
<b>8</b>	<b>EXPOSURE AND PERSONAL PROTECTION</b>	
	IN ACCORDANCE WITH GOOD INDUSTRIAL PRACTICE AND HANDLING USING STANDARD EYE PROTECTION. USE OF PROTECTIVE MASK FOR DUST PARTICLES.	
<b>9</b>	<b>PHYSICAL AND CHEMICAL PROPERTIES</b>	
	PHYSICAL FORM:	Waxy hardened granules
	COLOUR:	Yellow amber waxy hardened granules
	ODOUR:	Characteristic minimal
	BOILING POINT:	-
	MELTING POINT:	-
	VISCOSITY:	-
	FLASH POINT:	-
	FLAMMABILITY SOLID/GAS:	N/A
	AUTO FLAMMABILITY:	N/A
	SPECIFIC REFRACTIVE:	-
	EXPLOSIVE PROPERTIES:	N/A
	pH:	N/A
	OXIDIZING PROPERTIES:	N/A
	VAPOUR PRESSURE:	N/A
	DENSITY:	0.688 - 0.695
	WATER SOLUBILITY:	Soluble
	OTHER SOLUBILITY:	Soluble in most volatile cosmetic solvents
	BULK DENSITY:	0.688 - 0.695
	PARTITION COEFFICIENT: (OCTANOL/WATER)	-
	EXPLOSIVE LIMITS:	-
<b>10</b>	<b>STABILITY AND REACTIVITY</b>	
	THERMAL DECOMPOSITION:	Stable under normal conditions of use.
<b>11</b>	<b>TOXICOLOGICAL DATA</b>	Animal Tests Last Done 1992, as requirements of the then <b>EC DIRECTIVE 91/155/EEC</b>
	ORAL:	LD50 > 36,000 MG/KG (Body Wt.) Rat Essentially Non-Toxic and Edible in Small Quantity.
	DERMAL:	Expected To Be Essentially Non Toxic.
	INHALATION:	Slight Ethanolic Sting - irritation
	<b>SPECIFIC CONCENTRATION LIMITS M-FACTORS (EC REGULATION NO#1272/2008 AMENDED NO#790/2009) compliant to the GHS.</b>	36,000 MG/KG (Body Wt.); CATEGORY 5 Essentially Non-Toxic and Edible in Small Quantity.
	<b>TOXIC EFFECTS:</b>	



# Metabolism of Cofactors and Vitamins; Ubiquinone biosynthesis [MAP:00130]

Metabolism; Metabolism of Cofactors and Vitamins; Ubiquinone biosynthesis [MAP:00130]





## References:

- 1) B.O. Linn, A.C. Page, E.L. Wong, et al, *J Am Chem Soc* 1959; 81: 4007-4010.
- 2) F.L. Crane, Y. Hatefi, R.L. Lester, et al, *Biochim Biophys Acta* 1957; 25: 220- 221.
- 3) T. Kishi, T. Okamoto, H. Kishi, et al, In: K. Folkers and Y. Yamamura (eds.), *Biochemical and Clinical Aspects of Coenzyme Q*, Vol. 5. Elsevier Science Publishers, Amsterdam. 1985, p. 119-123.
- 4) P.M. Kidd, W. Huber, F. Summerfield, et al, *Coenzyme Q10: Essential Energy Carrier and Antioxidant*. H.K. Biomedical Consultants, Berkeley. 1988, p. 3.
- 5-a) See reference 3.
- 5-b) K. Folkers, T. Watanabe, M. Kaji, *J Mol Med* 1977; 2: 431-460.
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