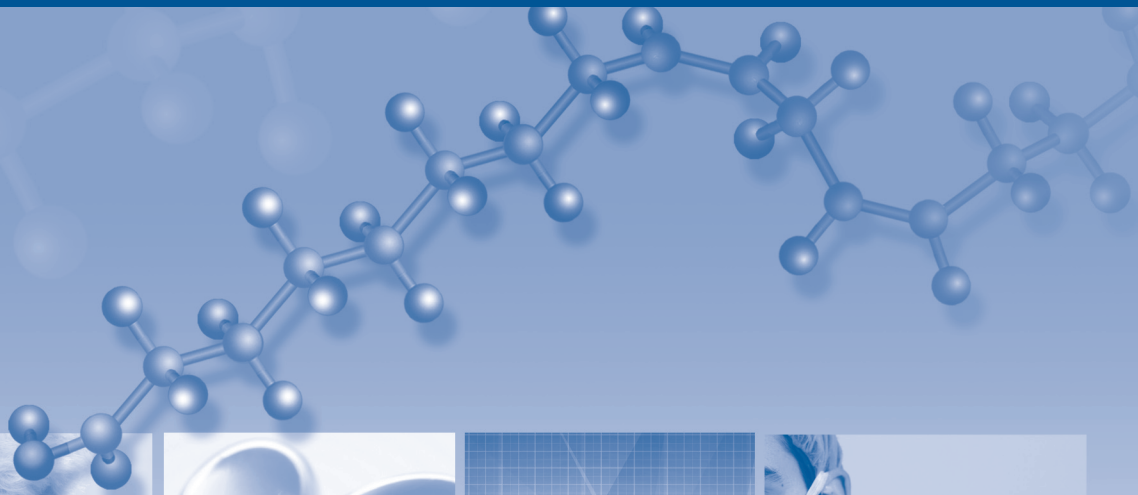


A CLINICAL HANDBOOK



Essential Fatty Acids in the healthcare practice

**NORDIC[®]
NATURALS** 
Pure and Great Tasting Omega Oils

CONTENTS

Introduction	1
I. What are Essential Fatty Acids (EFAs)	1
II. Sources of Essential Fatty Acids	1
III. Metabolism of Essential Fatty Acids	2
IV. Balance of Omega-6 to Omega-3 is Key to Good Health	3
V. Proven Benefits of Essential Fatty Acids	3
General Health and Well-Being	3
Cardiovascular Health	4
Cognitive Health	4
Anti-inflammatory	5
Pregnancy, Infancy, and Breast Feeding	5
Ocular Health	6
VI. Dose	7
VII. Safety of EFA Supplementation	8
VIII. Choosing a Fish Oil Supplement	8
Type of Fish Oil	8
Fish Oil Freshness	9
Fish Oil Quality Standards	9
Sustainably Harvested Fish Oil	9
References	10

INTRODUCTION

The information in this booklet is produced exclusively for healthcare professionals, and is not intended for consumers or patients. This publication is not intended as a substitute for medical therapy or as a manual for self-treatment. All readers should seek professional advice for any specific medical problem.

I. WHAT ARE ESSENTIAL FATTY ACIDS (EFAs)

The human body can manufacture most of the fats it needs, including cholesterol, saturated fatty acids, and unsaturated fatty acids. However, there are two families of fatty acids, the omega-6 and the omega-3 fatty acids, that are considered essential fatty acids. These fatty acids are essential because the parent omega-6 fatty acid, linoleic acid (LA), and the parent omega-3 fatty acid, alpha-linolenic acid (ALA), absolutely cannot be synthesized by the body and must be obtained from the diet or supplementation.

Omega-3 fatty acids are essential fatty acids that are necessary from conception through pregnancy, and continue to support normal growth and development of infants. Throughout life, omega-3 fats aid in the prevention and treatment of heart disease, diabetes, arthritis, inflammatory diseases, and cancer¹. Omega-3 fatty acids also play an important role in protecting the health of the brain, eyes, and nervous system.

Over 8,000 published clinical trials have unequivocally established that omega-3 fatty acids are important in human nutrition. This clinical guide is intended to provide the healthcare practitioner with a basic understanding of omega-3 fatty acids and how to best utilize their powerful health-promoting qualities in the clinical setting.

II. SOURCES OF ESSENTIAL FATTY ACIDS

The primary source of omega-6 fatty acids in the human diet is linoleic acid (LA) from the oils of seeds and grains. Sunflower, safflower, soy, and corn oils are particularly rich in linoleic acid. Evening primrose oil, borage oil, and black currant oil are unique due to their relatively high content of the health-promoting omega-6 fatty acid, gamma-linolenic acid (GLA).

The primary dietary source of omega-3 fatty acids is alpha-linolenic acid (ALA) from seeds and seed oils that are derived from plants such as flax, walnuts, and canola. Fish and fish oils are the richest source of preformed long chain omega-3 fatty acids, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA).

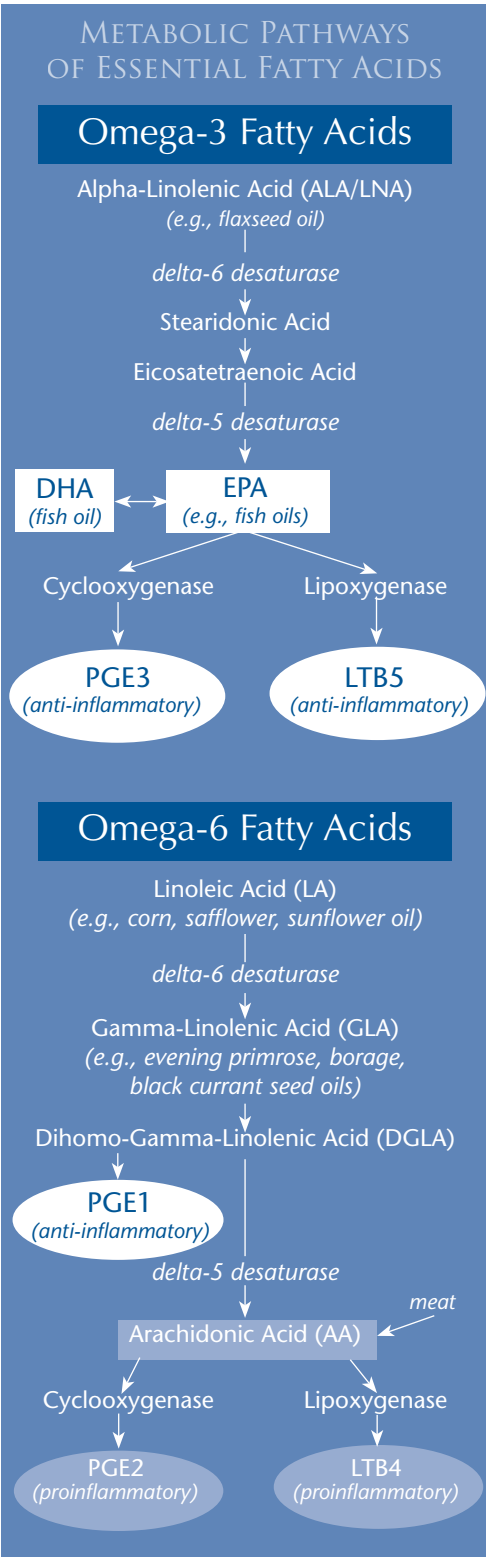
III. METABOLISM OF ESSENTIAL FATTY ACIDS

Through an inefficient enzymatic process, the parent omega-6 and omega-3 fatty acids, LA and ALA, can be elongated and desaturated into the functionally important longer chain omega-6 and omega-3 fatty acids. ALA (18 carbons) can be converted into a small amount of EPA (20 carbons) and even less DHA (22 carbons). Emken, *et al*, reported a 15% conversion of ALA to EPA. Whereas, Pawlosky, *et al*, found 0.2%. Both reported that the conversion to DHA was much less than that to EPA^{2,3}.

EPA and DHA are molecular precursors to a family of eicosanoids that are anti-inflammatory, antithrombotic, antiarrhythmic, and vasodilatory. The parent omega-6 fatty acid, LA, is converted to arachidonic acid (20 carbons), which is the precursor to a different group of eicosanoids that are proinflammatory and prothrombotic.

Omega-3 and omega-6 fatty acids compete for the same enzymes (delta-5 and delta-6 desaturase) for conversion into the longer chain omega-6 and omega-3 fats. The competition between the parent omega-6 and omega-3 fatty acids for conversion into the longer chain fatty acids is biologically important because eicosanoids are derived from Arachidonic Acid (AA) while eicosanoids derived from the omega-3s, EPA and DHA, have directly opposing effects. AA-derived eicosanoids are proinflammatory, and EPA-derived eicosanoids and DHA-derived resolvins are anti-inflammatory.

High intake of LA from vegetable oils such as corn, safflower, sunflower, and cottonseed has been shown to inhibit the conversion of ALA to the longer chain EPA and DHA. Because of the health-promoting effects of the long chain omega-3 fatty acids, EPA and DHA, and the relatively low rate of conversion from ALA, EPA and DHA are considered “conditionally essential fatty acids.” Currently there is a scientific consensus that adequate intake of fish and fish oil supplements that provide preformed EPA and DHA is important for the prevention of many common chronic disease states⁴. In addition, a large body of scientific evidence suggests that maintaining a balanced ratio of omega-6 to omega-3 fatty acids is essential for optimal health.



IV. BALANCE OF OMEGA-6 TO OMEGA-3 IS KEY TO GOOD HEALTH

Humans have evolved consuming a diet that contained approximately equal amounts of omega-3 and omega-6 fatty acids. About 100 years ago, the industrial revolution introduced technology that allowed for the refining of vegetable and seed oils, which led to a dramatic increase in the consumption of omega-6 fatty acids among the industrialized countries. In addition, the introduction of animal feeds derived from grains rich in omega-6 fats has resulted in the production of meat, fish, and eggs high in omega-6 fats and virtually void of omega-3 fats.

Today, in Western diets, the ratio of omega-6 to omega-3 fatty acids ranges from 20:1–30:1 instead of the pre-industrial range of 1–2:1⁵. A large body of scientific evidence has established that a high intake of omega-6 fatty acids shifts the physiological state to one that promotes thrombosis, vasoconstriction, inflammation, and poor cellular health. The physiologic changes that result from high intake of omega-6 fats has been implicated in pathophysiology of heart disease, diabetes, autoimmune and inflammatory diseases (rheumatoid arthritis, colitis ulcerosa, multiple sclerosis, lupus, asthma, etc.), depression, dementia, and other chronic diseases.

V. PROVEN BENEFITS OF ESSENTIAL FATTY ACIDS

1. General Health and Well-Being

A large body of scientific evidence suggests that aberrant inflammation underlies many common chronic diseases and is an obstacle to overall good health. The direct role of arachidonic acid-derived lipid mediators in promoting inflammation and EPA- and DHA-derived lipid mediators in regulating the resolution of inflammation has initiated much scientific interest in the influence of the omega-6:omega-3 ratio on human health.

In a population-based study involving 2,416 adolescents and adults living in New Zealand, there was a positive association between higher serum omega-3 concentration and physical well-being and self-reported mental well-being⁶. In addition, higher omega-3 intake is associated with:

- ◆ Improved mood⁷
- ◆ Healthy metabolism and body composition^{8,9}
- ◆ Bone strength¹⁰
- ◆ Memory¹¹
- ◆ Respiratory function¹²
- ◆ Skin health¹³
- ◆ Eye health¹⁴
- ◆ Attention and focus¹⁵

2. Cardiovascular Health

The most rigorous evidence supports using fish oil to benefit the hearts of healthy people, and those at high risk of, or who have, heart disease. Evidence from a multitude of large, well-conducted, controlled clinical trials demonstrate that omega-3 fats support cardiac health.

The evidence is so strong that the American Heart Association (AHA) considers increasing omega-3 fatty acids as a vital public health intervention, and encourages physicians to recommend their consumption. In fact, the AHA guidelines include recommendation for all Americans to consume omega-3-rich fish at least twice weekly. For individuals with documented heart disease, the AHA recommends 1 gram of EPA + DHA daily, and for patients with elevated triglycerides 2–4 grams of EPA+DHA daily.

Omega-3 fats have been shown to:

- ◆ Improve heart rate and rhythm¹⁶
- ◆ Reduce triglycerides¹⁷
- ◆ Reduce blood pressure¹⁸
- ◆ Lessen the effects of chronic inflammation on the heart and blood vessels¹⁹
- ◆ Reduce the risk of angina, heart attack, and stroke²⁰
- ◆ Reduce risk for co-morbidities of cardiovascular disease, including insulin resistance and metabolic syndrome²¹

3. Cognitive Health

Research has shown that omega-3 fats are necessary to develop, maintain, and protect structures of the central nervous system from conception through pregnancy and infancy and, undoubtedly, throughout life. There is some debate with regard to the relative importance of EPA versus DHA, but there is an overall scientific consensus that both EPA and DHA contribute to cognitive health and development as well as mental well-being, behavior, learning, and mood.

Most evidence suggests that DHA is particularly important for development of the brain and nervous system in infants, protection and repair of brain and nervous tissue from age-associated damage, and improving mental function.

Research suggests that **DHA** plays an important role in:

- ◆ Supporting fetal nervous system development in utero²²
- ◆ Improving cognitive function in infants, toddlers, and children²³
- ◆ Preventing dementia and Alzheimer's in the aging population²⁴
- ◆ Improving cognitive performance in individuals 70+ years of age²⁵.

Published clinical trials suggest that **EPA** has a particular affinity for conditions associated with altered mood and behavior including:

- ◆ Depression²⁶
- ◆ Bipolar disorder²⁷
- ◆ Schizophrenia²⁸
- ◆ ADHD²⁹

4. Anti-inflammatory

Inflammation is a normal protective physiological mechanism, but several factors in the Western diet, including excess omega-6 fat intake, and a relative deficiency of omega-3 fats, result in long-term inflammation. Omega-3 fatty acids from fish oil have anti-inflammatory effects due to the competition of EPA with AA in the cyclooxygenase and lipoxygenase pathways. In addition, omega-3s contribute to the formation of resolvins and protectins, which aid in the removal of inflammatory cells and restoration of tissue homeostasis once the need for inflammation is over.

Epidemiological evidence has demonstrated that EPA and DHA levels are decreased in patients who suffer from chronic pain and inflammation³⁰. Randomized controlled trials have demonstrated reduced morning stiffness and joint tenderness with regular oral intake of fish oil³¹.

Pharmacological anti-inflammatory drugs are effective in reducing inflammation but carry potentially dangerous side effects, rendering them impractical for long-term use. Several well-designed clinical trials have examined the use of fish oil on nonsteroidal anti-inflammatory drug (NSAIDS) use or steroid use in non-surgical back pain and rheumatoid arthritis. These trials show that fish oil consistently demonstrated a reduced requirement for anti-inflammatory drugs and improved clinical outcomes³². The anti-inflammatory benefits of fish oil are generally attained at a minimum dose of 3 grams of EPA +DHA and require 8 to 12 weeks of supplementation to realize these benefits.

Fish oil has been successfully used to in a range of conditions related to chronic inflammation including:

- ◆ Rheumatoid arthritis^{33, 34}
- ◆ Ankylosing spondylitis (chronic inflammation and potential fusion of the spine and sacroiliac joints)³⁵
- ◆ Back pain³⁶

5. Pregnancy, Infancy, and Breast Feeding

DHA is a significant structural component of the brain, eyes, and nervous system, which all are rapidly developing throughout the last trimester of pregnancy and the early stages of life. The fetus is dependent on its mother for DHA intake, which must be sufficient to maintain her own healthy levels and meet fetal demands, especially during the period of rapid nervous system development (last trimester–age 2)

Research has shown that fish oil supplementation improves DHA status of mothers and their breast milk, and infants³⁷.

Higher DHA status has been correlated with:

- ◆ Helping women to get pregnant³⁸
- ◆ Lowering the risk of premature births³⁹
- ◆ Reducing the risk of post-partum depression⁴⁰

Research has also shown that getting enough DHA during pregnancy improves the health of offspring in several ways.

- ◆ Studies show that DHA may improve behavior, attention, focus, and learning in children⁴¹
- ◆ Reduce the risk of allergies⁴²
- ◆ Positively influences immune development⁴³
- ◆ Increase indices of intelligence in babies and children⁴⁴
- ◆ Lower brain DHA levels are also associated with cognitive deficits and increased behavioral indicators of anxiety, aggression, and depression in children⁴⁵

In the US, Dietary Reference Intakes (DRI) for DHA during pregnancy have not been established. However, the world's leading experts on lipids and human nutrition have concluded that during pregnancy and lactation women must ensure a minimum DHA intake of 300 mg daily⁴⁶.

6. Ocular Health

Omega-3 fatty acids from fish oil help maintain healthy structure and function of ocular tissue. DHA is particularly important for the eyes, and attains its highest concentration anywhere in the body within the eye tissue⁴⁷. Certain unique biochemical characteristics of DHA make it vital for the development, function, and maintenance of the highly active, light-receiving cells found in the eye.

Research has shown that DHA is necessary to develop, maintain, and protect visual structures from conception through pregnancy, infancy, and throughout life.

- ◆ DHA supplemented during pregnancy plays a role in the maturation of the visual system, and DHA supplementation of infant formula supports visual acuity⁴⁸.
- ◆ Omega-3 fats support the body's natural anti-inflammatory response, which can alleviate many ocular symptoms including dryness, pain, redness, and lack of tear production⁴⁹.
- ◆ Higher intake of omega-3 fats is also associated with decreased likelihood of having age-related macular degeneration and cataracts⁵⁰.
- ◆ Consistent evidence suggests that omega-3 fats act in a protective role against light, oxygen, and age-associated damage to the eyes⁵¹.

VI. DOSE

Dosing is based on the amount of EPA and DHA in a product and not on the total amount of fish oil. Supplements vary in potency and the percentage of EPA and DHA in the oil.

Experts recommend between 500–1000 mg EPA and DHA per day to maintain health and avoid deficiency. Therapeutic doses of EPA and DHA range from 1–4 grams. To support the body’s anti-inflammatory response, clinical studies suggest a minimum of 3 grams of EPA and DHA with some studies using 10 grams or more.

Recommendations for Adding Omega-3 Fatty Acids to the Diet

The following chart gives a nice comparison for consumers, making it easier to understand what type of dosage is required when taking different concentrations and forms of fish oil products to achieve certain EPA/DHA requirements.

Column One: The first range of 500 mg of EPA and DHA is a basic, standard maintenance dose. It assumes that there are no major health issues, and is suitable as a daily recommendation for healthy individuals.

The second range of 1000 mg of EPA and DHA would be for those who have known risk factors for heart disease. *The American Heart Association (AHA) suggests this dosage for those with documented heart disease, while the American Psychiatric Association (APA) recommends this amount for individuals with mood disorders.*

The third range of 3000 mg of EPA and DHA is recommended to support the body’s natural anti-inflammatory response to support individuals with inflammatory conditions such as arthritis.

Column Two: Represents amount of an average size can of sardines (82 g≈1/3 cup) to achieve EPA/DHA daily recommendations.

Column Three: Represents dose of a fish body oil product in soft gels, non-concentrated, consisting of 18% EPA and 12% DHA.

Column Four: Represents dose of a fish body oil product in soft gels, concentrated, consisting of 35% EPA to 25% DHA.

Column Five: Represents dose of a fish body oil product in liquid, concentrated, consisting of 35% EPA to 25% DHA.

Column Six: Represents dose of a cod liver oil product in liquid, consisting of 9% EPA to 14% DHA.

EPA + DHA	CAN OF SARDINES	OMEGA-3 18:12	ULTIMATE OMEGA 35:25	ULTIMATE OMEGA LIQUID 35:25	ARCTIC COD LIVER OIL LIQUID 9:14
500 mg	1/4 can	2 soft gels	1 soft gel	<.25 tsp	.5 tsp
1000 mg	1/2 can	4 soft gels	2 soft gels	<.50 tsp	1 tsp
3000 mg	1 1/2 can	11 soft gels	6 soft gels	<1.25 tsp	3 tsp

VII. SAFETY OF EFA SUPPLEMENTATION

The US Food and Drug Administration (FDA) classified omega-3 fatty acids from fish oil as “generally recognized as safe” (GRAS)⁵². In fact, The FDA has ruled that up to 3g of EPA plus DHA is safe to be included in the food supply of Americans without fear of adverse events⁵³. In addition, there are no known significant drug interactions with omega-3 fatty acids⁵⁴. When using higher amounts of EPA and DHA in the clinical setting, it is important to monitor the use, efficacy, safety, and potential interactions.

The hemodynamic effects of omega-3 fatty acids have led to theoretical concerns about increased risk for bleeding at higher doses (above 3 grams EPA+DHA), if taken with blood thinning medications, or before surgery. The theoretical risk of clinically significant bleeding has not been verified in a controlled setting. A 2007 expert opinion published in the *American Journal of Cardiology* concluded that omega-3 fatty acid supplements do not increase the risk for clinically significant bleeding, even in patients also being treated with antiplatelet or anti-thrombotic medication⁵⁵. The therapeutic use of omega-3 fatty acids perioperatively to improve surgical outcomes and reduce adverse events is also the subject of current clinical investigations.

Increasing EPA and DHA intake through fish consumption alone is associated with the risk of consuming excess environmental toxins. The US Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) have warned the public about the potential dangers of consuming too much fish because of the associated toxins⁵⁶. The introduction of high quality fish oil supplements that have been processed to remove environmental contaminants allows for supplementation of high levels of EPA and DHA for preventive and therapeutic clinical use without the risk of toxicity. In studies that compare levels of mercury, organochlorines, and other environmental toxins commonly found in fish versus fish oil supplements have shown that fish oil does in fact provide the benefits of EPA and DHA without any associated environmental contaminants⁵⁸.

VIII. CHOOSING A FISH OIL SUPPLEMENT

1. Type of Fish Oil

Fish oil supplements vary in potency and/or percentage of EPA and DHA. There are two main types of non-concentrated fish oils. One is typically derived from the body of smaller pelagic fish such as sardines and anchovies and contains approximately 18% EPA and 12% DHA (18:12). The other non-concentrated fish oil is cod liver oil, which is derived from the liver of Cod and contains approximately 14% DHA and 9% EPA (14:9). Cod liver oil also contains naturally occurring fat-soluble vitamins A and D, which can fluctuate in concentration with seasonal shifts in food supply.

Concentrated fish oil products begin as non-concentrated fish body oil (18% EPA and 12% DHA). The native fish oil is taken through various manufacturing steps to modify the concentration and percentage of EPA and DHA. The levels of EPA and DHA can be raised from the initial 20–30% to between 60–90% EPA and DHA. A wide variety of concentrations and ratios of EPA and DHA are made available to increase patient compliance (less soft gels to achieve a therapeutic dose) and to target specific therapeutic needs.

Consumers are often unaware that concentrated fish oil products are manufactured in two distinctly different molecular forms: one containing synthetic ethyl esters and the other containing the re-assembled natural triglyceride structure. In making a fish oil concentrate, the individual fatty acids are first removed from the glycerol backbone; then they undergo molecular distillation that allows for the relative concentrations of EPA, DHA, and other naturally occurring fatty acids to be modified.

Once the desired amounts of fatty acids are achieved, a manufacturer chooses from two distinctly different options. The first is to use enzymes to reattach the fatty acids to the glycerol backbone in a process known as “re-esterification.” This process reassembles the fatty acids into the natural triglyceride structure.

The second, less costly manufacturing option is to react the free fatty acids with ethanol (CH₃CH₂OH). This results in an “ethyl ester” fatty acid, a fatty acid that does not occur naturally anywhere in the human diet⁵⁸. The majority of concentrated EPA and DHA products available to consumers today are in the ethyl ester form, perhaps due to the lower cost of production. Although the majority of fish oil products on the market contain the ethyl ester form of EPA and DHA, current research evidence suggests the triglyceride form is better for absorption and assimilation.

2. Fish Oil Freshness

Fish oil is meant to be fresh, just like fish. The biggest problem with deterioration in the quality of a fish oil product is rancidity, which results in a distinct rank taste and smell, and fishy eructations (fishy burps). The main cause of rancidity is oxidative free radical damage to the double bonds found in EPA and DHA. Taste is directly correlated to freshness and lack of oxidative damage to the oil. To achieve the benefits of fish oil, it is important to choose a fresh, great-tasting fish oil that does not repeat.

The most common analytical assessments of oxidation are provided in terms of Peroxide Value (PV), Anisidine Value (AV) and Totox Value. These values are considered objective measures of fish oil freshness, with lower values representing less oxidation.

The therapeutic action and safety of fish oil is in part related to its molecular stability and resistance to oxidative damage. Fish oil that has been subject to oxidative damage may do more harm to the body than good.⁵⁹

3. Fish Oil Quality Standards

Because there are no fish oil quality standards in the United States, individuals must determine what standards a manufacturer is voluntarily following—if any—to ensure a fish oil is pure, fresh, and without contamination. The highest standards in the industry today are the Norwegian Medicinal Standard (NMS) and the European Pharmacopoeia Standard (EPS). By following these standards a manufacturer can guarantee quality products by measuring potency and setting maximum allowances on peroxide, anisidine, and totox levels and heavy metals, dioxins, furans, Polychlorinated biphenyl (PCBs), and other environmental contaminants.

4. Sustainably Harvested Fish Oil

Overfishing is a serious global issue that threatens the health of the world’s oceans. The United Nations estimates that about three-quarters of the planet’s fish stocks are now fished to their maximum limits or already exhausted. An environmentally responsible fish oil manufacturer should offer transparency into their fishing practices. Any manufacturer committed to sustainability will only harvest fish species that are not endangered, and only from waters that are not overfished. A manufacturer should also ensure that 100% of all fish harvested are utilized for human or animal consumption.

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