Neptune Krill Oil (NKO™)

Human Safety Assessment

Report to:

NEPTUNE TECHNOLOGIES & BIORESSOURCES INC.

Department of
Research & Development

Submitted by:

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1.0 Background

Neptune Krill Oil™ is a complex natural health product extracted from a crustacean, habitant of the Antarctic Ocean known as the Antarctic Krill (Euphausia superba). In general, this product consists of a natural blend of polyunsaturated fatty acids, phospholipids, antioxidants, metals and minerals.

Neptune Krill Oil is intended for human consumption as a dietary supplement, beneficial for the maintenance of a normal and healthy function of body systems.

2.0 Safety Assessment:

2.1 Study Objectives

The objective of the present studies was to investigate the possible toxicity of consumption of Neptune Krill Oil (NKO™) in humans by determining a variety of physical, biochemical and hematological variables. These variables reflect kidney, liver, pancreatic, and hematological, respiratory, intestinal, musculoskeletal and general biological function.

2.2 Long Term Safety Assessment / Animal studies:

2.2.1 Study Design

This was a prospective controlled trial where all animals were submitted to a high dose of NKO™.

2.2.2 Animal model:

The animal model used was C57BL6 Nude Congenic Mice – B6NU-T heterozygote.

Mice were kept in a controlled environment with a 12 hour regulated light – dark cycle.

2.2.3 Treatment:

Animal dose: 16.6% daily diet or 3g per 21.94cm^2 mean body surface

Human equivalent: 9 grams of EPA and DHA per day (70 kg person) which corresponds to 23.1 grams of oil or 7 – 11 times the recommended dose.

Duration: 6 months

Method: All animals were evaluated weekly by a certified vetenerian. At the end of 6 months all animals euthanized by gas exposure and all organs were submitted to histopathological analysis

2.2.4 Results:

Clinical observations: No adverse effects reported

Pathology results: autopsies performed on all systems revealed no pathological findings. The following organs were examined:

a. Brain
b. Lungs
c. Heart
d. Stomach
e. Pancreas
f. Liver
g. Kidneys

h. Uterus / prostate

i. Intestine

j. Skin

3.0 Hman Safety Assessment:

3.1 Study Design

This was a prospective controlled trial where all patients were submitted to a high dose of NKO™.

3.2 Patients

The study enrolled 25 healthy volunteers, 13 women and 12 men aged between 25 and 53 years, with a mean age of 42.

3.3 Materials & Methods

All volunteers were advised to take NKO™ 2 gelcaps three times per day for 2 months. Each gelcap contained 1 gram of NKO™.

3.3.1 NKO™ Contents

Component	mg / gelcap	mg / 6 gelcaps
Omega-3	386	2 316
Phospholipids	416	2 496
Astaxanthin	0.16	0.96

All participants were advised to continue with their usual nutrition habits and to refrain from initiating any special diet.

3.4 Outcome Measures

3.4.1 General Parameters tested

1. Upon initiation:
   a. Complete blood count and biochemical blood test
   b. Vital signs
   c. Medical history
2. Every month:
   a. Monitoring of vital signs
   b. Complete blood count and biochemical blood test
   c. Adverse events / Regurgitation

3.4.2 Biochemical parameters tested (analyzed at an independent laboratory):

a. Complete blood count
b. PTT
c. Creatinine
d. Glucose
e. Alkaline Phosphatase
f. Albumin
g. Amylase
h. Bilirubin total

i. Bilirubin direct

j. Cholesterol

k. Triglycerides

l. HDL + LDL

m. Cholesterol / HDL ratio

n. Urea

o. TSH

Patients were advised to stop if they notice any of the following symptoms occurring without a logical reason:

a. Low blood pressure (< 90/65)

b. High blood pressure (3 or more points above your usual blood pressure)

c. Difficulty breathing

d. Bleeding

e. Loss of consciousness (faint, dizzy)

f. Unusual migraines

g. Unusual body pain

h. Fatigue, weakness

i. Weight gain

j. Significant alterations in your blood test

3.5 Results:

- ✓ No serious side effects were observed.
- ✓ Of the25 healthy volunteers enrolled in the study, one female patient with known salt intolerance withdrew due to a moderate increase in water accumulation.
- ✓ Of the remaining 24 patients two women complained of rapidly increasing greasiness of their facial skin and requested to be withdrawn from the study.
- ✓ The 22 remaining volunteers completed the 2-month period without any noticeable physical or laboratory adverse events.
- ✓ Among the 25 healthy volunteers participating in the trial there were no complaints of regurgitation or unpleasant aftertaste.

3.5.1 Observed benefits:

- ✓ Increased ability to concentrate
- ✓ Decreased seasonal allergy symptoms
- ✓ Increased skin hydration
- ✓ Improved hair texture
- ✓ Decreased joint discomfort
- ✓ Minimized PMS emotional and physical symptomatology

The table below describes the changes in the laboratory tests between the baseline and follow up assessments:

Parameter:	Mean Change Baseline – Follow UP	Std. Deviation	95% Confidence Interval of the Difference		P Value
			Lower	Upper	
Hemoglobin	1.9565	6.65704	-.9222	4.8352	.173
Hematocrit	.0179	.01775	.0172	.0176	.6994
Platelets	-14.2174	53.77390	-37.4710	9.0362	.218
PTT	1.3391	3.96023	-.3734	3.0517	.119
Glucose	.0883	.65303	-.1941	.3707	.524
Urea	.0652	.84294	-.2993	.4297	.714
Creatinine	7.4348	7.25061	5.0021	9.8675	.650
Cholesterol	***.4675***	***.65512***	***.1909***	***.7441***	***.002***
Triglycerides	***.1937***	***.36865***	***.0381***	***.3494***	***.017***
HDL	***-.1387***	***.21955***	***-.2315***	***-.0460***	***.005***
LDL	***.3662***	***.70315***	***.0693***	***.6632***	***.018***
CHOL/HDL	***.5604***	***.72054***	***.2562***	***.8647***	***.001***
Albumin	***1.4091***	***2.64861***	***.2348***	***2.5834***	***.021***

Bilirubin Total	.2174	1.95301	-.6272	1.0619	.599
Bilirubin Direct	-.1182	.42047	-.3046	.0682	.202
ALPP	1.1818	8.30741	-2.5015	4.8651	.512
GGT1	.9565	9.97943	-3.3589	5.2719	.650
Amylase	***3.4348***	***5.07960***	***1.2382***	***5.6314***	***.004***
NA	.5000	2.01778	-.3946	1.3946	.258
K	-.1545	.58369	-.4133	.1042	.228
TSH	-.0354	.40912	-.2216	.1508	.696

These results show that the values for following parameters: Cholesterol, LDL, Albumin and Amylase decreased significantly during the study. For HDL there was a statistically significant increase between baseline and the final follow up. There were no adverse events observed in the study sample. These results show that NKO™ is well tolerated without any expected adverse reactions when consumed on a high dose by humans.

3.6 Conclusion:

The results of the present toxicity assessment confirm that Neptune Krill Oil (NKO™) can be considered as safe for human consumption even at double the highest recommended dose.

Note: People with a known allergy to fish or seafood were not tested in this study. The precaution remains that in the case of the above allergies, previous professional allergy testing is advised prior to consumption of Neptune Krill Oil (NKO™).