Top Ten Things to Know
n-3 Polyunsaturated Fatty Acid ("Fish Oil") Supplementation
and the Prevention of Clinical Cardiovascular Disease

1. Approximately 85.6 million American adults have cardiovascular disease (CVD), including 15.5 million with coronary heart disease (CHD). CVD costs about $316.6 billion dollars annually (2012 dollars).¹

2. Based on nationally representative survey data, a recent analysis unaffiliated with the American Heart Association estimated that omega-3 fatty acids were the most commonly used non-vitamin/non-mineral supplement in the United States in 2011-2012 and that the prevalence of omega-3 fatty acids from fish oil supplements increased almost 7-fold from 1.3% in 1999-2000 to 12% in 2011-2012.²

3. In 2002, the American Heart Association published a Scientific Statement, Fish Consumption, Fish Oil, Omega-3 Fatty Acids and Cardiovascular Disease which recommended that patients with documented coronary heart disease (CHD) consume ≈ 1 g/d of EPA + DHA, preferably from oily fish, but EPA + DHA supplements could be considered in consultation with a physician.³ Several RCTs have been conducted since the 2002 Statement evaluating the effects of supplementation of EPA + DHA on the occurrence of clinical CVD.

4. The authors reviewed published clinical data from randomized controlled trials (RCTs) for several conditions including: prevention of CVD mortality in Diabetes/Prediabetes, prevention of CHD among patients at high CVD risk, Secondary Prevention of CHD and Sudden Cardiac Death (SCD) among Patients with Prevalent CHD, Primary or Secondary Prevention of Stroke, Secondary Prevention of Outcomes in Patients with Heart Failure, Secondary Prevention of Atrial Fibrillation in Patients with Prior Atrial Fibrillation, and Atrial Fibrillation following Cardiac Surgery.

5. Based on the data currently available, treatment with n-3 Polyunsaturated Fatty Acid supplements is reasonable for two conditions:
   - Secondary Prevention of CHD and Sudden Cardiac Death (SCD) among patients with Prevalent CHD
   - Secondary Prevention of Outcomes in Patients with Heart Failure.

6. Based on the data currently available from randomized controlled trials, treatment with n-3 Polyunsaturated Fatty Acid supplements is not indicated for the following five conditions:
   - Prevention of CVD Mortality in Diabetes/prediabetes
   - Prevention of CHD among patients at High CVD Risk (mixed populations with and without CHD)
   - Primary Prevention of stroke (High CVD risk (with or without prevalent CHD))
   - Secondary Prevention of Atrial Fibrillation in Patients with Prior Atrial Fibrillation
   - Atrial fibrillation following Cardiac Surgery.


7. Many of the studies reviewed in this Advisory used relatively low doses of n-3 Polyunsaturated Fatty Acid supplements, however higher dose trials are ongoing and may provide more robust results for certain conditions. The authors note that “lack of evidence of a benefit differs from evidence of a lack of effect.”

8. There were no reports from clinical trials for fish oil supplements in the primary prevention of CHD, Primary Prevention of Heart Failure, or Primary Prevention of Atrial Fibrillation. No recommendations were made for these populations at this time, however the results from ongoing RCTs may inform future recommendations related to these potential indications for n-3 PUFA supplementation.

9. The risk of major adverse effects, such as bleeding and stroke, associated with n-3 PUFA supplementation was low in the RCTs of clinical cardiovascular outcomes reviewed in this Advisory. In this context of uncertain benefit but no apparent major risk, patient preferences should also influence clinical decisions.

10. While recent RCT evidence has raised questions about the benefits of n-3 supplementation to prevent clinical cardiovascular disease events, the recommendation for patients with prevalent CHD, such as a recent myocardial infarction remains essentially unchanged: treatment with n-3 PUFA supplements is reasonable for these patients. Even a potential modest reduction in CHD mortality (10%) in this clinical population would justify treatment with a relatively safe therapy.