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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

THAMAR SANTISTEBAN CORTINA, on behalf of herself, all others similarly situated and the general public,

Plaintiff,

v.

WAL-MART STORES, INC., and LANG PHARMA NUTRITION, INC.,

Defendants.

Case No: 3:13-cv-02054-BAS-DHB

CLASS ACTION

SECOND AMENDED COMPLAINT FOR:

VIOLATIONS OF THE MAGNUSON-MOSS WARRANTY ACT;

VIOLATIONS OF CALIFORNIA CONSUMER PROTECTION STATUTES; AND

BREACHES OF EXPRESS AND IMPLIED WARRANTIES

DEMAND FOR JURY TRIAL

Upon defendant Wal-Mart Stores, Inc.'s written consent pursuant to Fed. R. Civ. P. 15(a)(2), plaintiff Thamar Santisteban Cortina hereby files this Second Amended Complaint and, on behalf of herself, all others similarly situated, and the general public, by and through her undersigned counsel, hereby sues Wal-Mart and Lang Pharma Nutrition, Inc., and alleges the following upon her own knowledge, or where she lacks personal knowledge, upon information and belief, and the investigation of her counsel.

INTRODUCTION

1. Coenzyme Q10 is a nutrient with proven health benefits, but also a well-known drawback: it is not soluble in water, and poorly soluble in fat. This is problematic for consumers who use CoQ10 supplements because the body and digestive tract are aqueous, and the absorption of a substance depends on its first dissolving. To address this problem, some dietary supplement manufacturers have invented technologies for modifying orally-administered CoQ10 to increase its solubility, and thereby its bioavailability.

2. Wal-Mart markets and sells a store-brand dietary CoQ10 supplement called "Equate High Absorption Co-Q10." Wal-Mart represents on Equate's packaging that it "Helps support Heart Health," "Supports heart and vascular health," "Promotes healthy blood pressure levels," is "Essential for energy production," is "Beneficial to Statin Drug Users," and provides "Powerful natural antioxidants." Equate's packaging also says it offers "clinical strength," "high absorption," and "3x better absorption." And Wal-Mart represents that Equate is comparable to a competing brand-name CoQ10 supplement, by stating expressly on Equate's label that consumers can "Compare to Qunol™ Ultra CoQ-10," by placing Equate immediately next to Qunol on Wal-Mart's retail shelves, and by modeling Equate's numerical claim, "3x better absorption," on Qunol's identical claim. A true and correct copy of Equate's packaging is attached hereto as Exhibit 1.

3. Lang supplies Equate to Wal-Mart. Together, Lang and Wal-Mart conceived, devised, and created Equate's packaging, including its claims and representations, and put Equate into the stream of interstate commerce for sale to the consuming public, reasonably expecting the consuming public to rely on the product claims.

4. Wal-Mart and Lang's statements are false and misleading. Laboratory tests demonstrate the Equate CoQ10 softgels frequently fail even to rupture within 15 minutes, the time designated for effectiveness by the U.S. Pharmacopeial Convention (USP), the organization that sets testing standards in the dietary supplement industry. Instead, the softgels sometimes do not rupture after more than 30, 45, or even 60 minutes. Thus, Equate frequently will pass through a consumer's digestive tract without *any* dissolution or absorption; or, if rupture occurs late, dissolution and hence absorption will be substantially diminished. Laboratory tests also show that Equate exhibits substantially less than the 75% dissolution minimally necessary for effectiveness, also as designated by the USP. Moreover, a significant disparity in testing results suggests Equate is manufactured without adequate quality control, meaning consumers cannot obtain, much less expect, consistent and predictable results from one bottle of Equate to the next.

5. Rupture is the first step in dissolution, and dissolution the first step in absorption; thus because of Equate's rupture problems and substandard dissolution, it cannot possibly provide the "clinical strength," "high absorption," and "3x better absorption" Wal-Mart and Lang claim, nor the claimed health benefits.

6. Wal-Mart and Lang's comparison of Equate to Qunol is also false and misleading. First, the products are formulated differently and employ different technologies for increasing CoQ10 absorption. Second, in apples-to-apples testing, a laboratory blindly tested samples of Equate and Qunol purchased at the same time, from the same Wal-Mart retail store, using the same tests and techniques promulgated by the USP. In a standard rupture test using water, Qunol ruptured in 13 minutes, while Equate did not rupture even after 60 minutes. Similarly, Qunol dissolved 92.7% in water, while Equate dissolved less than 2%. Even in a retest using pepsin, an enzyme that aids dissolution, Equate took 47 minutes to rupture and dissolved only 45.3%. The results of the Equate testing are consistent with at least four other tests conducted by three other independent testing laboratories between August 2013 and February 2014.

7. Plaintiff brings this class action to remedy the damage caused to her and other consumers by Wal-Mart's false advertising, aided and abetted by Lang, and defective Equate CoQ10 product.

JURISDICTION & VENUE

8. The Court has original jurisdiction pursuant to 28 U.S.C. § 1331 because this action raises a federal question under the Magnuson-Moss Warranty Act, 15 U.S.C. §§ 2301 *et seq.* The Court also has original jurisdiction pursuant to 28 U.S.C. § 1332(d)(2), the Class Action Fairness Act, because the matter in controversy exceeds the sum or value of $5,000,000 exclusive of interest and costs and because more than two-thirds of the members of the classes reside in states other than the states in which Defendants are citizens.

9. Venue is proper in this Court pursuant to 28 U.S.C. § 1391 because plaintiff resides in and suffered injuries as a result of Wal-Mart and Lang's acts in this district, many of the acts and transactions giving rise to this action occurred in this district; and because Wal-Mart and Lang are authorized to conduct business in this district, do substantial business in this district, have intentionally availed themselves of the laws and markets of this district, and are subject to personal jurisdiction in this district.

PARTIES

10. Plaintiff Thamar Santisteban Cortina is a resident of Bonita, California, in San Diego County.

11. Defendant Wal-Mart Stores, Inc. is a Delaware corporation with its principal place of business at 702 Southwest 8th Street, Bentonville, Arkansas 72716.

12. Defendant Lang Pharma Nutrition, Inc. is a Rhode Island corporation with its principal place of business at 20 Silva Lane, Middletown, Rhode Island 02842.

FACTS

A. Coenzyme Q10

13. CoQ10 is a vitamin-like, anti-oxidant nutrient produced naturally in the heart, liver, kidneys, and pancreas. It plays a vital role in cellular energy production and is known to provide various benefits, especially to heart health. Although most commonly known in

abbreviated form as CoQ10, it is more formally referred to as ubiquinone, ubidecarenone, or uniquinol, depending upon its form.

14. Although the body generally produces sufficient CoQ10, blood levels can be depleted by aging, heart disease, and some medications, especially statins. For those wishing to replace depleted CoQ10 or otherwise increase blood levels to realize the substance's potential health benefits, dietary supplementation is common.

15. In order to provide a benefit, a nutrient must first be absorbed into the body's systemic circulation in an adequate amount. Thereafter, it is carried to various organs and tissues for eventual uptake by the cells. Accordingly, to realize any benefits of CoQ10 supplementation at a cellular level, an individual must achieve effective or optimum CoQ10 blood levels. In its raw form, however, CoQ10 is a crystalline powder that is insoluble in water, and poorly soluble in fat. It has been reported that the bioavailability[1] of raw CoQ10 powder is less than 10%.

16. The formulation of a CoQ10 dietary supplement is crucial to its bioavailability. CoQ10 supplements have been available to consumers for approximately 20 years, but initial CoQ10 supplements offered on the market, which were little more than raw CoQ10 powder, were not well-absorbed because of CoQ10's hydrophobicity and large molecular weight. It has long been known that the absorbability of CoQ10 can be increased when taken with food. The absorption of poor water-soluble drugs—that is fat soluble vitamins like CoQ10—is increased especially when administered with or after a meal containing fat, in part because fats stimulate bile salt secretion, which assists in drug and vitamin solubilization because bile salts are natural emulsifiers. However, taking such unsophisticated CoQ10 supplements with food does not, alone, significantly enhance absorption.

17. CoQ10 is a commodity product, with hundreds of different brands on the market. Like plaintiff, consumers of CoQ10 supplements—who are familiar both with

[1] Bioavailability is the propensity of a substance to reach the systemic circulation, which decreases with incomplete absorption (by comparison, medicine intravenously injected is 100% bioavailable).

CoQ10's benefits, and its poor absorption—seek out technologies that purport to increase its absorbability. Thus, according to NAD, in December 2009, "several manufacturers currently advertise 'absorbability' as one of the features of their CoQ10 supplements."

18. Over the past several years, dietary supplement manufacturers have taken a variety of approaches to boosting the bioavailability of orally-administered CoQ10 supplements—some as simple as suspending CoQ10 powder in oil, others complex, patented processes—with varying degrees of success. Examples of patented technologies employed in some different CoQ10 supplements include Bio-Solv and Hydro-Q-Sorb (Tishcon Corp.), Q-Sorb (Nature's Bounty), All-Q (DSM Nutritional Products Ltd.), and VESIsorb (Source One Global Partners, LLC).

19. Because the body is comprised far more of water than fat, in order to enhance the substance's dissolution, and thus absorbability, companies seriously seeking to enhance CoQ10 dissolution and absorption try to make the compound maximally water-soluble.

20. CoQ10 is one of the most popular supplements in the United States, with sales over $500 million in 2011.

B. The United States Pharmacopeial Convention

21. USP is a nonprofit scientific organization founded in 1820 in Washington, D.C., whose participants, working under strict conflict-of-interest rules, and using careful scientific method and consensus, set enforceable standards for the quality of drugs, and voluntary standards for the quality of vitamins and dietary supplements. Known as Reference Standards, these are updated and published annually jointly by USP and the National Formulary in a compendia known as USP-NF.

22. Although compliance with USP's standards concerning dietary supplements is not required by regulation, USP plays a major role in the multi-billion dollar dietary supplement industry, providing the objective (and only) scientifically-valid industry standards against which all supplements may be tested and measured, providing important information about a supplement's intrinsic qualities, and serving as a "level playing field" for

comparing two or more products, *despite* that manufacturers are not required by law to meet them.

23. Compliance with an applicable USP monograph means a tested product contains the ingredients listed in the declared amount and potency, and will break down and release into the body within a specified amount of time. Thus, whether or not required by regulation, the testing and measurement of a dietary supplement by the prescribed USP methodologies and standards provides an objective idea of whether the supplement is likely to be effective when taken orally by a human.

24. Information that can be gleaned from USP testing is important to consumers in determining the relative quality (and value) of competing dietary supplements. For example, in a product review of joint health supplements for pets and animals containing glucosamine, chondroitin, and MSM, ConsumerLab.com, a well-respect consumer watchdog organization that does comparative testing, the company noted that certain formulations "were analyzed for disintegration utilizing [USP] <2040> recommendations," and to obtain a "Pass," a product must "meet recommended USP <2040> parameters for disintegration for dietary supplements[.]"

25. In the case of CoQ10 softgels, the USP tests for rupture and dissolution show whether a product is likely to break up early enough in the digestive process to provide an effective amount of the enclosed CoQ10, and, if the product does timely rupture, whether the vitamin is likely to adequately dissolve so as to provide substantial bioavailability.

26. The process of digesting a CoQ10 softgel supplement begins with the timely rupture, or break up, of the gelatin outer shell. This is a necessary prerequisite to absorption because a pill that does not timely rupture will pass through the gastrointestinal tract without dissolution and then absorption commencing as quickly, or at all. Digestion is a relatively quick process, and in some cases, a softgel may *never* rupture. A person consuming such a capsule would pass it without digesting or absorbing any of its contents, realizing *none* of the product's potential benefits or value.

27. Even if a CoQ10 softgel ruptures, for effectiveness it must adequately dissolve, because dissolution is the first step in, and a prerequisite to, the absorption of a vitamin. Thus, information about a supplement's dissolution rate provides an accurate idea of how effective a supplement is likely to be when it is orally ingested.

28. The USP-NF compendia consists of Monographs, General Chapters, and General Notices. Monographs include the name of an ingredient or preparation; its definition; its packaging, storage, and labeling requirements; and its specification, which consists of a series of tests, procedures for the tests, and acceptance criteria that require use of the official USP Reference Standards. General Chapters set forth tests and procedures referred to in multiple monographs. And General Notices provide definitions for terms used in monographs, as well as information necessary to interpret monograph requirements.

29. A true and correct copy of the USP Monograph for CoQ10, designated "Ubidecarenone Capsules" ("USP CoQ10 Monograph"), is attached hereto as Exhibit 2, and expressly incorporated into this Complaint.

30. The USP CoQ10 Monograph prescribes the following "Performance Tests": "**Disintegration and Dissolution <2040>:** Meet the requirements of the test for *Disintegration*, except where the product is labeled to contain a water-soluble form of ubidecarenone. Capsules labeled to contain a water-soluble form of ubidecarenone meet the requirements for *Dissolution* as follows." The Monograph then sets forth a procedure and method of calculation, and requires that "NLT [Not Less Than] 75% of the labeled amount of ubidecarenone . . . dissolve[s]."

31. The tests for *Disintegration* (sometimes called Rupture) and *Dissolution* (sometimes called solubilization) are set forth in the USP-NF General Chapter on Disintegration and Dissolution of Dietary Supplements, USP-NF General Chapter <2040>, a true and correct copy of which is attached hereto as Exhibit 3, and expressly incorporated into this Complaint. Although Chapter <2040> includes sections on both *Disintegration* and *Dissolution*, the specific dissolution procedure set forth in the USP CoQ10 Monograph supplements or replaces the dissolution section in Chapter <2040>. For *Disintegration*,

Chapter <2040> requires "Soft Shell Capsules," like the VESIsorb CoQ10 softgels and Qunol softgels, to "[p]roceed as directed under *Rupture Test for Soft Shell Capsules*," which in turn requires rupture "in not more than 15 minutes."

32. In 2014, USP <2040> was revised to add the following paragraph (with emphasis added) in its Introduction:

> Disintegration and dissolution tests as described in this chapter are quality-control tools to assess performance characteristics of dietary supplement finished dosage forms. These performance standards are intended to detect problems that may arise due to use or misuse, or changes in coatings, lubricants, disintegrants, and other components. ***These performance tests are also intended to detect manufacturing process issues such as over-compression and over-drying that would affect the release characteristics of the final dosage forms.*** These tests are not intended to be used as a demonstration or as a surrogate for in vivo absorption, bioavailability, or effectiveness, unless an in vitro-in vivo correlation (IVIVC) has been established.

33. Finally, the USP CoQ10 Monograph requires that, "[w]here the product contains a water-soluble form of ubidecarenone, this is so stated on the label."

C. Equate CoQ10

34. Wal-Mart purchases Equate from Rhode Island supplier Lang. Together, Wal-Mart and Lang conceived, devised, and created Equate's packaging, including its claims and representations, which Wal-Mart presents to the consuming public at its retail locations.

35. Lang supplies CoQ10 softgels identical to those in Equate to other retailers including CVS/pharmacy, which sells the CoQ10 softgels under its store brand, calling them "CVS/pharmacy Ultra CoQ10," and Walgreens, which sells them under its store brand, calling them "Well Enhanced Absorption CoQ10."

36. The CoQ10 softgels supplied by Lang for use in Wal-Mart Equate, CVS Ultra, and Walgreens Well employ a patented technology for delivering vitamins called VESIsorb.

Accordingly, both the Equate CoQ10 softgels and CVS Ultra CoQ10 softgels are sometimes referred to below as the "VESIsorb CoQ10 softgels."

37. The VESIsorb technology was invented by Swiss company Vesifact, AG. The intellectual property, however, is owned by SourceOne, a Chicago company, which licenses it to Lang for use in the VESIsorb CoQ10 softgels.

38. Lang outsources manufacturing of the VESIsorb CoQ10 softgels to a Florida company called Swiss Caps USA, Inc. Lang sends Swiss Caps both raw CoQ10 powder, and raw VESIsorb "paste." Swiss Caps then mixes the two and encapsulates the resulting "medicine" in a gelatin softgel. Swiss Caps ships the completed softgels back to Lang, which packages them (for example, in either Wal-Mart Equate, CVS Ultra, or Walgreens Well packaging), and distributes the completed product to its customers, shelf-ready for sale to consumers.

39. The VESIsorb technology is described in U.S. Patent No. 8,158,134, a true and correct copy of which is attached hereto as Exhibit 4 and expressly incorporated into the Complaint; and German Patent No. EP1249230B1, a true and correct copy of which is attached hereto as Exhibit 5 and expressly incorporated into the Complaint.

40. VESIsorb's U.S. patent states that the "invention relates to compositions in the form of microemulsion preconcentrates," which, "[w]hen contacted with water or with an aqueous medium . . . form microemulsions," which themselves, when "[i]n the aqueous phase, . . . may contain water-soluble substances."

41. SourceOne's website for VESIsorb quotes a Dr. Andrew Halpner as saying of VESIsorb, that its "ability to offer bio-enhanced, water-soluble ingredients such as CoQ10 . . . to dietary supplement, functional food and beverage markets, has set a new benchmark for the industry."[2] On the same page, SourceOne depicts a product called "Pure encapsulations Ubiquinol VESIsorb." A brochure for the product states that the VESIsorb technology

[2] *See*, "Products Offered / VESIsorb Delivery System," at http://source-1-global.com/products-offered/vesisorb-delivery-system (last visited July 28, 2014).

"increases bioavailability of a bioactive that is fat soluble or that has poor water solubility," by creating "[n]anosized water-soluble droplets" that "allow the bioactive to cross the water layer of the GI tract for absorption."

42. In an effort to prove its technology, Vesifact commissioned a study to compare the bioavailability of CoQ10 capsules made with VESIsorb to other commercially-available CoQ10 supplements. The results were reported in the March-April issue of Alternative Therapies in Health & Medicine, in an article titled *Relative Bioavailability Comparison of Different Coenzyme Q10 Formulations with a Novel Delivery System*,[3] a true and correct copy of which is attached hereto as Exhibit 6, and expressly incorporated into this Complaint.

43. *Relative Bioavailability* describes the VESIsorb "delivery system" as "a lipid-based formulation that self-assembles on contact with an aqueous phase into a colloidal delivery system," which it says is an example of "enhancement of the rate and extent of dissolution," rather than "facilitation of an absorption process."

44. Equate's packaging (*see* Ex. 1) makes the following representations:

a. The Benefit Claims:

- "Helps support Heart Health"
- "Supports heart and vascular health"
- "Promotes health blood pressure levels"
- "Essential for energy production"
- "Beneficial to Statin Drug Users"
- "Powerful natural antioxidants"

b. The Efficacy Claims:

- "Clinical Strength"
- "High Absorption"
- "3 times better absorption"

[3] Z. Xia-Lui et al., *Relative Bioavailability Comparison of Different Coenzyme Q10 Formulations with a Novel Delivery System,* Alternative Therapies in Health & Medicine 15(2) 2009, 42-46.

c. The Comparative Claim:

- "Compare to Qunol™ Ultra CoQ-10"

45. Equate's comparative claim is bolstered by Wal-Mart's practice and policy of placing Equate immediately next to Qunol on its retail shelves. Moreover, Equate's "3x better absorption" claim is modeled on Qunol's identical claim, which was in the marketplace long before Equate. And Equate's packaging contains several claims identical or substantially similar to claims that first appeared on Qunol's packaging.[4] The sum effect of Equate's comparative packaging claim and Wal-Mart and Lang's related sales practices is to suggest that Equate is a store-brand or generic version of the brand-name Qunol product, perhaps identically formulated (as with many store-brands and generics), and offering the same benefits.

46. Although the Equate CoQ10 softgels are based on the VESIsorb technology that purports to make the CoQ10 nutrient water-soluble, and thus contain a water-soluble form of ubidecarenone, this is not stated on Equate's label. This may be an attempt to avoid the USP CoQ10 Monograph's special dissolution requirement for water-soluble forms of ubidecarenone. This is, however, a Catch-22 for Wal-Mart and Lang, because if its position is that Equate is in fact *not* a water-soluble form of CoQ10, this is effectively an admission that Equate does *not* offer "high absorption" CoQ10, since it is well-established that the bioavailability of lipid-based forms of CoQ10 is simply not on par with hydro-soluble versions like Qunol. In short, water solubility is the gold standard of CoQ10 absorption and bioavailability.

D. Qunol CoQ10

47. Qunol is sold by Quten Research Institute, LLC, a New Jersey company. The technology employed in enhancing dissolution of the so-called "Q-Gel" CoQ10 (a trade

[4] Qunol's packaging includes the following claims: "Clinical Strength," "3X Better Absorption," "Supports heart and vascular health," "Promotes healthy blood pressure levels," "Essential for energy production," "Beneficial to Statin drug users," and "Powerful all-natural antioxidant."

name) in Qunol softgels is described in U.S. Patent Nos. 6,056,971, 6,300,377, and 6,740,338, and registered under the trademark, "Bio-Solv." The process used to manufacture Qunol produces sub-micron size CoQ10 molecules, increasing the surface area of the CoQ10, and thereby enhancing its interaction with bile salts, for enhanced micellization and absorption. This makes Qunol water-soluble. Qunol is also formulated with 150 IU of Vitamin E, which enhances the solubility of its CoQ10. Qunol's packaging, a true and correct copy of which is attached hereto as Exhibit 7 and expressly incorporated into the Complaint, notes that Qunol passes the USP dissolution test and is both water- and fat-soluble.

E. Plaintiff's Purchases

48. Plaintiff has used CoQ10 supplements since 2008.

49. On several occasions, plaintiff purchased Equate at the Wal-Mart located at 1360 Eastlake Parkway, Chula Vista, California, 91915, or at the Wal-Mart located at 1200 Highland Avenue, National City, California, 91950. Plaintiff's most recent Equate purchase was in mid-July, 2013.

50. Before ever purchasing Equate, plaintiff was familiar with, and had previously purchased Qunol. She believed it was a good and effective product, and purchased Equate in substantial part because Wal-Mart compares Equate to Qunol, but sells Equate for a few dollars less, thus appearing to provide a better value.

51. For each Equate purchase, plaintiff relied on Wal-Mart and Lang's representation that Equate provides "clinical strength," "high absorption," and "3 times better absorption" than competing products, that it is comparable to more expensive brands like Qunol, and that it generally supports heart health.

F. Independent Laboratory Testing

52. The Lang-supplied VESIsorb CoQ10 softgels that Wal-Mart sells as Equate have been subject to numerous tests in 2013 and 2014, including by both plaintiff and Lang, sometimes on behalf of Wal-Mart or CVS. Several tests show USP failures. By contrast, in an apples-to-apples comparison, Qunol showed far superior results to Equate.

1. Eurofins Testing (July 2014)

53. From about July 7 to 21, 2014, Eurofins Scientific, Inc.'s Supplement Analysis Center in Petaluma, California tested: (a) a sample of Equate, from Lot G13NM13, bearing an expiration date of March 2015, which was purchased on August 15, 2013 from the Wal-Mart located at 4840 Shawline St., San Diego, California 92111; and (b) a sample of Qunol, from Lot 1341-2121, bearing an expiration date of March 2016, that was also purchased on August 15, 2013 from the Wal-Mart located at 4840 Shawline Street, San Diego, California 92111. From August 2013 to July 2014, the samples were maintained, sealed in the bottles, alongside one another, each in its outer cardboard packaging, inside a file cabinet, in an office whose temperature is generally maintained between 69 and 74 degrees Fahrenheit. The Equate and Qunol samples were provided to Eurofins blindly, in sealed bottles whose labels were completely obscured. Eurofins tested both samples for rupture and dissolution according to the methods prescribed by USP. Eurofins testing shows Equate failed to rupture after more than 60 minutes in water, and took 47 minutes to rupture during a retest using pepsin, an enzyme that breaks down proteins and promotes solubilization. The Qunol sample ruptured in 13 minutes in water. The Eurofins testing also shows the Equate sample achieved less than 2% dissolution in water, compared to 92.7% dissolution for Qunol. On a retest using pepsin, Equate achieved 45.3% dissolution. A true and correct copy of the July 21, 2014 Eurofins Certificates of Analysis for Equate Lot G13NM13, and Qunol Lot 1341-2121, are attached hereto as Exhibit 8.

2. Advanced Botanical Testing (February 2014)

54. On August 8, 2012, Advanced Botanical Consulting & Testing, Inc. received from Lang a sample of CVS Ultra softgels (e.g., the same VESIsorb CoQ10 softgels as Equate) for a long-term stability study. The sample was identified as "Lot #: F12NM10." At 18 months, in February 2014, Advanced Botanical tested Equate's "Rupture (USP)." The results: "Fail, >30 min." Advanced Botanical had not previously tested for rupture since receiving the sample in August 2012. A true and correct copy of the Advanced Botanical testing report, dated February 18, 2014, is attached hereto as Exhibit 9.

3. Tampa Bay Analytical Research Testing (November 2013)

55. On November 18, 2013, Tampa Bay Analytical Research, Inc. (TBAR) tested samples from two different lots of CVS Ultra CoQ10, Lots F12NM09 and F12NM10, which are the identical Lang-supplied VESIsorb CoQ10 softgels as in Equate. The samples were purchased on June 9, 2013 (Lot F12NM09), and August 15, 2013 (Lot F12NM10), from the CVS/pharmacy store located at 4829 Clairemont Drive, San Diego, California, 92117. From June and August 2013, respectively, until early November 2013, the samples were maintained, sealed in the bottles, in their outer cardboard packaging, in an office whose temperature is generally maintained between 69 and 74 degrees Fahrenheit. The samples were provided to TBAR blindly, in sealed bottles whose labels were completely obscured. For each lot, TBAR analyzed 6 capsules, following USP protocols for testing rupture and dissolution. TBAR's testing showed that 7 out of 12 of the soft gel capsules tested did not rupture at all, even after 60 minutes; 3 out of the 12 experienced at best an immaterial, *de minimis* leakage of contents, perhaps from a pinhole-size opening, but no discernable, visible rupture was observed, even after 60 minutes; and only 2 softgel capsules (1 from each lot) actually ruptured, but only after approximately 50 minutes. The 2 capsules that ruptured showed only 27.6%, and 27.9% dissolution. A true and correct copy of TBAR's two testing reports, each an "Assay Result Form," is attached hereto as Exhibit 10.

4. Advanced Botanical Testing (September 2013)

56. Between September 6, 2013 and September 10, 2013, Advanced Botanical performed USP dissolution testing for Lang on a sample identified as "CoQ10 w/ VesiSorb," and identified as "Item#: C13NM29," with an expiration date of January 2015. This corresponds to Equate CoQ10 that was available for purchase in around June 2013, for example, in the Wal-Mart located at 4840 Shawline St., San Diego, California 92111. Using the standard USP procedure, Advanced Botanical's testing showed Equate achieved only 39% dissolution. The report describes the reason for the poor dissolution:

> CoQ10 in the softgels once ruptured was physically suspended in the dissolution medium, not chemically solublized. If the solution is directly

> filtered and injected, the unsolublized portion is removed by the filtration step, which lead to low result. The dissolution sample needs to be properly diluted with organic solvent like isopropyl alcohol to assure complete solublization of the CoQ10, prior to injection into the HPLC.

The USP methods and procedures applicable to CoQ10 do not permit the use of isopropyl alcohol to enhance CoQ10 dissolution. A true and correct copy of Advanced Botanical's September 10, 2013 testing report as described above is attached hereto as Exhibit 11.

5. Covance Testing (August 2013)

57. Between August 2 and 12, 2013, Covance Laboratories analyzed samples from two different lots of Equate. Following USP procedures, for each lot Covance measured six softgels, determining that one lot offered an average of 41.18% dissolution, and the second, and average of 41.3% dissolution. A true and correct copy of the Covance Laboratories Certificates of Analysis relating to this testing (one per lot) are attached hereto as Exhibit 12.

* * *

58. The preceding testing results concerning rupture and dissolution are summarized in the following table:

	Qunol	***Equate***				
Test	**Eurofins (7/14)**	**Eurofins (7/14)**	**ABC (2/14)**	**TBAR (11/13)**	**ABC (9/13)**	**Covance (8/13)**
Disintegration	13 min	> 60 min (47 min w/ pepsin retest)	> 30 min	> 60 min (10 capsules); 50 min (2 capsules)	-	-
Dissolution	92.7%	< 2% (45.3% w/ pepsin retest)	-	27.75% (avg)	39%	41.24% (avg)

WAL-MART AND LANG'S DECEPTIVE ACTS & UNFAIR BUSINESS PRACTICES

A. Wal-Mart Sells Defective Equate CoQ10 Dietary Supplements

59. In some cases, Equate softgels do not rupture within 15, or even 30, or 45, or even 60 minutes, providing consumers with little or no benefit, making them ineffective, and indeed defective. But even if Equate occasionally timely ruptures, it fails to adequately

dissolve, at best exhibiting less than 50% dissolution, well below the USP standard of 75%, further providing little or no benefit to consumers, also rendering the product defective.

60. CoQ10 supplements manufactured in full compliance with Good Manufacturing Practices, and exercising adequate quality control, will measure far more consistently than does the Equate across batches and lots, and over time (e.g., without degradation during the product's lifetime preceding its expiration date). The wide divergence in Equate's dissolution results—less than 2%, 28%, 39%, 41%, 45%—suggest some defect in its formulation, manufacturing (including possibly relating to its outer softgel gelatin coating), packaging, or distribution resulting in inconsistent batches of Equate CoQ10, many of which provide the consumer little or no effect, and which may degrade quickly during the product's shelf life.

B. Wal-Mart and Lang's Claims of "High Absorption" and "3 Times Better Absorption" Are False & Misleading

61. Wal-Mart and Lang's efficacy claims of "High Absorption" and "3 Times Better Absorption" are based on the *Relative Bioavailability* study. On Equate's packaging, however, Wal-Mart and Lang deceptively omit the source of these claims, providing consumers with no means of investigating the claim's *bona fides*. Unsurprisingly, *Relative Bioavailability* does not establish Wal-Mart and Lang's claims.

62. First, *Relative Bioavailability's* small sample size (just 20 subjects) allows for distortion by random chance, and magnifies bias. This is especially true because the human body is a complex environment. Thus, the results cannot possibly be considered reliable.

63. Second, *Relative Bioavailability* employed improper exclusion criteria. Equate's packaging advertises it is "Beneficial to Statin Drug Users," but *Relative Bioavailability* excluded as test subjects those taking "Medication affecting cholesterol (eg, statins)." CoQ10 is often taken by those with heart conditions seeking to improve and promote heart health, and the Equate package states it "Helps support Hearth Health," but *Relative Bioavailability* excluded subjects with heart conditions. And while CoQ10 supplements are most popular with those over 55, *Relative Bioavailability* excluded subjects over 60, and did not state the age of the subjects chosen. The exclusion of test subjects with certain conditions and

characteristics undermines the study's reliability in predicting the "real world" absorption claimed by Wal-Mart on Equate's label.

64. Moreover, *Relative Bioavailability* represents only limited initial results with no verification of clinical response. The article concludes that "[a]dditional clinical studies are indicated to verify that the improved absorption with [VESIsorb] correlated with clinical response to treatment." Thus, by its own admission, the *Relative Bioavailability* study does not actually "verify" anything, and certainly not any "clinical response" to VESIsorb CoQ10 softgels, especially when extrapolated to the general population.

65. *Relative Bioavailability* is also undermined by bias and sponsorship, and cannot be considered independent. Besides Vesifact supplying the VESIsorb capsules for use in the study, "[t]he work was funded by Vesifact AG, Baar, Switzerland." And one of the two authors of the study, Carl Artmann, "served as paid consultant[ ] to Vesifact in monitoring and analyzing this study . . . ." The other author, Zheng-Xian Liu, "served as a paid consultant to SourceOne Global Partners in the preparation of th[e] manuscript . . . ." Despite stating that both authors of the study hold "no other financial interest in the products or technologies studied or in either Vesifact or SourceOne," the study's having been funded by and conducted on behalf of companies that in fact have a significant financial interest in its outcome undermines the study's credibility and reliability. And at the time Dr. Liu was paid by SourceOne to prepare the *Relative Bioavailability* manuscript, he had an ongoing relationship with, and was being compensated as a consultant on several different projects for SourceOne.

66. But even if *Relative Bioavailability* supported the conclusion that the VESIsorb capsules tested in Germany in 2008—likely fresh samples, carefully-manufactured by someone other than Swiss Caps, provided directly to the study's administrators by Vesifact—exhibited increased absorption, this does not support *Wal-Mart's* claim that *Equate*, as formulated, mass-manufactured, and distributed in the United States and available on retail shelves to consumers, offers equivalent "high" or "3 times" absorption.

67. To the contrary, a substantial body of testing based on USP protocols and standards shows Equate frequently fails to time rupture or rupture at all, offering consumers

little or no efficacy, and inadequately dissolves, making little CoQ10 even available for absorption and bioavailability.

68. This is especially significant because *Relative Bioavailability* discusses the importance of water solubility and the technology purportedly employed in Equate claims to enhance the water solubility of CoQ10, yet the USP test designed by independent scientists to determine whether a CoQ10 supplement is water soluble—the special dissolution test prescribed in the USP CoQ10 Monograph requiring 75% dissolution to pass—shows Equate not only consistently fails dissolution, but sometimes fails miserably: less than 2% dissolution.

69. For example, *Relative Bioavailability* explains that bile salts "enhance drug solubilization" because they help form "micelles" that "transport the lipophilic molecules though the aqueous environment of the gastrointestinal (GI) tract and across the unstirred water layer to the absorptive epithelium," and that VESIsorb supposedly "mimics this natural absorption process to improve bioavailability of poorly water-soluble drugs" like CoQ10.

70. As *Relative Bioavailability* notes "[t]he absorption of most drugs depends on 2 processes: (1) the dissolution fo the drug in physiological fluids and (2) the absoprtion process itself (ie, the process by which a drug in solution enters the cells at the absorption site and finally enters general blood circulation).") Thus in sum, "the dissolution of [a] drug is the first step in the absorption process . . . ." For poorly-absorbed drugs like CoQ10, one technique used to "increase the extent to which the administered drug is absorbed" is "enhancement of the rate and extent of dissolution," with VESIsorb an "example of the . . . technique."

71. *Relative Bioavailability* also notes that "VESIsorb was designed to address the poor bioavailability of . . . natural bioactives like CoQ10 exhibiting poor water solubility," by using a process in which the "bioactive will be solubilized . . . ."

72. If *Relative Bioavailability* requires water solubility in order for a CoQ10 supplement using VESIsorb technology to properly function, and industry standard testing based on sound scientifically-sound principles developed by an independent expert

organization demonstrates Equate is not water soluble, then by definition *Relative Bioavailability* cannot support Equate's claims of enhanced absorption (even if, *arguendo*, the study might otherwise support the claim for a VESIsorb-based CoQ10 supplement that practiced the patented technology correctly and was free from any formulation, manufacturing, or handling errors or defects).

73. The falsity of Wal-Mart's "high" and "3 times" claims is also demonstrable by comparison to Qunol, which also makes a "3X Better Absorption" claim. Qunol timely ruptures and exhibits more than 90% dissolution. In 2009, in response to a challenge by the Council for Responsible Nutrition, the National Advertising Division[5] investigated Qunol's "3X" claim, and held the claim was adequately supported.[6] If Qunol's "3X" claim is legitimate and substantiated where the product exhibits near-total dissolution, a product like Equate, which shows only 2%, or 28%, or 39%, or 41%, or 45% dissolution, cannot *similarly* offer "high" and "3 times" better absorption.

74. Wal-Mart and Lang also deceptively omit what products Equate offers "3 times better absorption" than. If Wal-Mart and Lang use the claim to suggest an equivalence to

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[5] The NAD is a division of the Council of Better Business Bureaus, whose policy and procedures are established by the Advertising Self-Regulatory Council (ASRC). NAD's mission is to review national advertising for truthfulness and accuracy, and thereby foster public confidence in the credibility of advertising. NAD reviews a case when an advertisement is challenged (usually by a competitor), with NAD's attorneys working with both parties' in-house counsel, marketing executives, and research and development departments, as well as with outside consultants, to decide whether the challenged claims have been substantiated. Each party is also given substantial time and opportunity to explain its position and provide supporting data. ASRC maintains a database of NAD case reports on its website.

[6] NAD noted that in response to its investigation Qunol's manufacture "submitted several published and unpublished studies which, it maintained, substantiate the enhanced bioavailability of the hydrosoluble CoQ10 in Qunol," and also "submitted a laboratory report . . . substantiating [Qunol's] hydrosolubility (i.e., that it passes USP Dissolution Test)" and "submitted reports of tests conducted on other CoQ10 softgel brands . . . that it maintained, indicated their lack of solubility, as shown by their lack of dissolution in the USP Dissolution Test."

Qunol, that is false and misleading for the reasons set forth herein. If Wal-Mart and Lang use the claim to compare Equate to *all* or *any given* CoQ10 dietary supplement in the market, this is also false: even *Relative Bioavailability* only compared the VESIsorb product to three others, and no other clinical studies comparing any other products to competing CoQ10 supplements—much less any studies comparing them to Equate, itself—have been conducted; by comparison, Qunol only claims to offer "3X better absorption" than "regular CoQ10," which its packaging defines as "unsolubilized Ubiquinone in oil suspensions and/or powder-filled capsules/tablets," based on specific studies performed relating to those specific products. But if Wal-Mart and Lang intend the "3 times better absorption" claim to make a comparison to regular, unsolubilized CoQ10 similarly to Qunol, this is also false because Equate fails the USP dissolution test just as any such "regular," unsolubilized CoQ10 supplement inevitably will.

C. Wal-Mart and Lang's Claims of "Clinical Strength" Are False & Misleading

75. When a product is touted as providing "clinical" results or strength, consumers believe that means the product has been shown, in a clinical trial, to be effective. For example, NAD has ruled even the statement that "a supplement has been 'used in several clinical studies' can be reasonably understood by consumers to mean that it has been studied *and* shown to be efficacious."

76. There are no clinical studies testing the efficacy of Equate CoQ10, as formulated, mass-manufactured, and available to consumers on Wal-Mart shelves.

77. Instead, Wal-Mart and Lang base their "Clinical Strength" claim on *Relative Bioavailability*. But whatever that study's results, a substantial body of independent laboratory testing, including testing commissioned by Equate's supplier, Lang, including on behalf of Wal-Mart, shows that because it fails to rupture and adequately dissolve, Equate, as formulated, and as available to consumers on retail shelves after mass-manufacturing and distribution in the U.S., is not of comparable quality to that tested in *Relative Bioavailability*,

and does not offer the "clinical" results or "strength" otherwise possibly suggested by *Relative Bioavailability*.

D. Wal-Mart and Lang's Benefit Claims Are False & Misleading

78. While Wal-Mart and Lang's benefit claims (like "Helps support Heart Health" and "Promotes healthy blood pressure levels") may be literally true since CoQ10 *can* offer such benefits if supplements are carefully formulated, manufactured, and handled, defects in Equate's formulation, manufacturing, or distribution chain resulting in CoQ10 softgels with frequent rupture failures and suboptimal dissolution, render the statements as used on Equate misleading, especially in combination with other efficacy and comparative claims.

E. Wal-Mart and Lang's Comparison to Qunol is False & Misleading

79. Qunol is a highly-respected, "high end" or "name" brand CoQ10 supplement, well-known to CoQ10 consumers. Its Q-Gel-branded CoQ10 supplements have been shown to effectively increase absorption in at least five bioavailability studies, and its "3X" claim has been investigated and upheld by the NAD.

80. Wal-Mart and Lang represent that Equate is comparable to the leading CoQ10 product on the market, by stating on its packaging "Compare to Qunol™ Ultra CoQ-10." This comparative claim is bolstered by Wal-Mart and Lang using packaging deceptively similar to that of Qunol, and by Wal-Mart and Lang's practice of placing Equate immediately next to Qunol on its retail shelves. The packaging of Equate contains several claims identical or substantially similar to claims that first appeared on Qunol's packaging.[7] The sum effect of Wal-Mart and Lang's comparative claim, package design and product placement is to suggest that Equate is a store-brand or generic version of the brand-name Qunol product, perhaps identically formulated (as with many store-brands and generics), and/or at the very least offering the same benefits.

[7] Qunol's packaging includes the following claims: "Supports heart and vascular health," "Promotes healthy blood pressure levels," "Essential for energy production," "Beneficial to Statin drug users," and "Powerful all-natural antioxidant."

81. But Wal-Mart and Lang's statement comparing Equate to Qunol is false because testing shows that Qunol, unlike Equate, timely ruptures, and offers substantially more dissolution than Equate: at most, Equate offers only half the dissolution of Qunol and thus simply cannot, like Qunol, offer "3 times better absorption" than competing products. The products are also formulated differently and employ different techniques to solve the CoQ10 dissolution problem. For example, Qunol includes 150 International Units (IU) of Vitamin E to promote solubility, while Equate contains only 10 IU of Vitamin E (in the form of d-alpha Tocopherol) (which Wal-Mart and Lang do not even disclose).

F. Equate is Misbranded

82. Wal-Mart and Lang misbrand Equate in violation of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 *et seq.*, and the California Sherman Food, Drug, and Cosmetic Law, Cal. Health & Safety Code §§ 109875 *et seq.*

83. Wal-Mart and Lang add 10 IU of Vitamin E (33.3% of the RDI) to Equate for purposes of supplementation. Wal-Mart and Lang also make a claim about Vitamin E by identifying its presence in Equate's ingredient list, as "d-alpha Tocopherol."

84. The FDCA requires a dietary supplement manufacturer who adds any vitamin or mineral listed in 21 C.F.R. § 101.9(c)(8)(iv) for purposes of supplementation, or makes a claim about any such vitamin or mineral, to declare the amount per serving and percent daily value. 21 C.F.R. 101.36(b)(2).

85. Accordingly, Equate is misbranded within the meaning of 21 U.S.C. §§ 343(e)(2) & (f).

86. For the reasons set forth herein, Equate is also misbranded because "its labeling is false or misleading in any particular," 21 U.S.C. § 343(a).

87. The California Sherman Law incorporates FDCA regulations into state law, Cal. Health & Safety Code § 110100, and also prohibits the sale of dietary supplements deemed misbranded under the federal laws and regulations (and thus under state law). Accordingly, Equate is misbranded under California state law.

PLAINTIFF'S RELIANCE AND INJURY

88. For her Equate purchases, plaintiff relied on Wal-Mart and Lang's representation that Equate provides "clinical strength," "high absorption," and "3 times better absorption" than competing products, that it is comparable to Qunol, and that it generally supports heart health, but these claims were false and misleading for the reasons described herein.

89. Because it frequently fails even to rupture, Equate is actually ineffective, so plaintiff did not receive what she paid for, and lost money in the full amount of her Equate purchases. Even where Equate ruptures, because it fails to adequately dissolve, Equate is actually only partially effective, so plaintiff did not receive what she paid for, and lost money in amount of her Equate purchases or some portion thereof.

90. Plaintiff purchased Equate instead of competing products based on the false statements and misrepresentations described herein.

91. Equate was unsatisfactory to plaintiff because it did not provide the full benefit advertised, and may have provided no benefit.

92. Plaintiff would not have purchased Equate absent Wal-Mart and Lang's misleading benefit, efficacy, and comparative claims, or she would not have paid the price she did for Equate, which is a little less expensive than Qunol, if she knew that Equate does not rupture at all or timely, does not dissolve at all or to any substantial degree (and certainly far less than the industry standard as reflected in the USP CoQ10 Monograph), and does not provide "high" or "3 times better" absorption than other brands of which she was aware and may have otherwise purchased.

93. Plaintiff would not have paid the price she did for Equate, and may not have been willing to purchase Equate at all, if she knew that it frequently fails to timely rupture, and provides substantially less dissolution than the USP CoQ10 Monograph specifies.

94. Plaintiff paid a price premium due to Wal-Mart and Lang's fraudulent conduct, in that Wal-Mart was able to command a higher price in the marketplace for Equate than it

otherwise could have absent its false and misleading benefit, efficacy, and comparative claims.

CLASS ACTION ALLEGATIONS

95. Pursuant to Rule 23, plaintiff seeks to represent a nationwide class comprised of all persons in the United States who purchased Equate primarily for personal, family, or household use, and not for resale, and a California subclass comprised of all persons in California who purchased Equate primarily for personal, family, or household use, and not for resale.

96. The members in the proposed class and subclass are so numerous that individual joinder of all members is impracticable, and the disposition of the claims of all class members in a single action will provide substantial benefits to the parties and Court.

97. Questions of law and fact common to plaintiff and the class include:

A. Whether Equate is a consumer product, whether the class members are consumers, and whether Wal-Mart is a supplier and warrantor, within the meaning of the Magnuson-Moss Warranty Act, 15 U.S.C. § 2301;

B. Whether through Equate's packaging claims, Wal-Mart made express or implied warranties to purchasers;

C. Whether Wal-Mart breached express warranties by failing to provide Equate in conformance with promises or descriptions that became a basis for the bargain;

D. Whether Wal-Mart breached implied warranties by failing to provide merchantable goods in selling Equate to the class members, or by selling Equate that was not fit for its particular purpose of supplementing the body's natural CoQ10 production sufficiently to support heart health and benefit statin users;

E. Whether Equate has actually malfunctioned or a defect manifested itself;

F. Whether Wal-Mart or Lang made statements, or aided and abetted the making of statements that were likely to deceive the public, concerning Equate's absorption and effectiveness;

G. Whether Wal-Mart or Lang made any statement, or aided and abetted the making of any statement, they knew or should have known was false or misleading;

H. Whether any of Wal-Mart or Lang's practices were immoral, unethical, unscrupulous, or substantially injurious to consumers;

I. Whether the utility of any of Wal-Mart or Lang's practices, if any, outweighed the gravity of the harm to its victims;

J. Whether Wal-Mart or Lang's conduct violated public policy as declared by specific constitutional, statutory or regulatory provisions;

K. Whether the consumer injury caused by Wal-Mart or Lang's conduct was substantial, not outweighed by benefits to consumers or competition, and not one consumers themselves could reasonably have avoided;

L. Whether Wal-Mart or Lang's conduct or any of their acts or practices violated the Magnuson-Moss Warranty Act, 15 U.S.C. §§ 2103 *et seq.*, the Lanham Act, 15 U.S.C. §§ 1051 *et seq.*, the California False Advertising Law, Cal. Bus. & Prof. Code §§ 17500 *et seq.*, the California Consumers Legal Remedies Act, Cal. Civ. Code §§ 1750 *et seq.*; the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 *et seq.*; the California Sherman Law, Cal. Health & Safety Code §§ 109875 *et seq.*; or any other law;

M. Whether Wal-Mart or Lang's policies, acts, and practices with respect to Equate were designed to, and did result in the purchase and use of Equate by the class members primarily for personal, family, or household purposes;

N. Whether Wal-Mart or Lang misrepresented or aided and abetted the misrepresenting of the source, sponsorship, approval, or certification of Equate within the meaning of Cal. Civ. Code § 1770(a)(2);

O. Whether Wal-Mart or Lang misrepresented or aided and abetted the misrepresenting of Equate's affiliation, connection, or association with, or certification by, another, within the meaning of Cal. Civ. Code § 1770(a)(3);

P. Whether Wal-Mart or Lang represented or aided and abetted the making of a representation that Equate has characteristics, uses, or benefits which it does not have, within the meaning of Cal. Civ. Code § 1770(a)(5);

Q. Whether Wal-Mart or Lang represented or aided and abetted the making of a representation that Equate is original or new if it has deteriorated unreasonably or is altered, within the meaning of Cal. Civ. Code § 1770(a)(6);

R. Whether Wal-Mart or Lang represented or aided and abetted the making of a representation that Equate is of a particular standard, quality, or grade, when it was really of another, within the meaning of Cal. Civ. Code § 1770(a)(7);

S. Whether Wal-Mart or Lang disparaged or aided and abetted the disparaging of the goods, services, or business of another by false or misleading representation of fact, within the meaning of Cal. Civ. Code § 1770(a)(8);

T. Whether Wal-Mart or Lang advertised or aided and abetted the advertising of Equate with the intent not to sell it as advertised, within the meaning of Cal. Civ. Code § 1770(a)(9);

U. Whether Wal-Mart or Lang represented or aided and abetted the making of a representation that Equate has been supplied in accordance with a previous representation when it has not, within the meaning of Cal. Civ. Code § 1770(a)(16)

V. The proper equitable and injunctive relief;

W. The proper amount of actual or compensatory damages;

X. The proper amount of restitution or disgorgement;

Y. The proper amount of punitive damages; and

Z. The proper amount of reasonable litigation expenses and attorneys' fees.

98. Plaintiff's claims are typical of class members' claims in that they are based on the same underlying facts, events, and circumstances relating to Wal-Mart and Lang's conduct.

99. Plaintiff will fairly and adequate represent and protect the interests of the class, has no interests incompatible with the interests of the class, and has retained counsel competent and experienced in class action litigation.

100. The class is sufficiently numerous, as both the class and subclass contain at least thousands of members who purchased the Wal-Mart Equate at issue in this action.

101. Class treatment is superior to other options for resolution of the controversy because the relief sought for each class member is small such that, absent representative litigation, it would be infeasible for class members to redress the wrongs done to them.

102. Questions of law and fact common to the class predominate over any questions affecting only individual class members.

103. As a result of the foregoing, class treatment is appropriate under Fed. R. Civ. P. 23(a), (b)(2), and (b)(3).

FIRST CAUSE OF ACTION

VIOLATIONS OF THE MAGNUSON-MOSS WARRANTY ACT,

15 U.S.C. §§ 2301 *ET SEQ.*

(By the Nationwide Class Against Wal-Mart)

104. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

105. Equate is a consumer product within the meaning of 15 U.S.C. § 2301(1).

106. Plaintiff and the class members are consumers within the meaning of 15 U.S.C. § 2301(3).

107. Defendant Wal-Mart is a supplier and warrantor as defined in 15 U.S.C. §§ 2301(4) & (5).

108. The Magnuson-Moss Warranty Act permits a consumer to recover damages caused "by the failure of a supplier, warrantor, or service contractor to comply with any

obligation under his [Act], or under a written warranty, implied warranty, or service contract." 15 U.S.C. § 2310(d)(1).

109. Wal-Mart's claims that Equate provides "clinical strength," "high absorption," and "3 times better absorption" is a "written warranty" within the meaning of the Act because it is an "affirmation of fact or written promise made in connection with the sale of" the product, "which relates to the nature of the material . . . and affirms or promises that such material . . . is defect free or will meet a specified level of performance . . . ." 15 U.S.C. § 2301(6)(A).

110. As set forth herein, Equate does not provide "clinical strength," "high absorption," or "3 times better absorption," as warranted.

111. Although Equate does not meet the "clinical strength"/"high absorption"/"3 times better absorption" specification, Wal-Mart has so far failed to refund Equate's purchasers their money.

112. By reason of Wal-Mart's breach of these express written warranties, Wal-Mart has violated the statutory rights due plaintiff and the class members pursuant to the Magnuson-Moss Warranty Act, thereby damaging plaintiffs and the class members. 15 U.S.C. §§ 2301 *et seq.*

113. Plaintiffs and the class were injured as a direct and proximate result of Wal-Mart's breach because: (a) they would not have purchased Equate on the same terms if they had known the true facts concerning its purported "better absorption"; (b) they paid a price premium due to Wal-Mart's misleading representations that Equate provides increased absorption, and (c) Equate does not perform as promised.

114. Plaintiff, on behalf of herself and the class members, seeks damages, equitable relief, and attorney's fees and costs pursuant to 15 U.S.C. §§ 2310(d)(1)-(2).

SECOND CAUSE OF ACTION

VIOLATIONS OF THE CALIFORNIA UNFAIR COMPETITION LAW, CAL. BUS. & PROF. CODE §§ 17200 *ET SEQ.*

(By the California Subclass Against Wal-Mart & Lang)

115. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

116. The UCL prohibits any "unlawful, unfair or fraudulent business act or practice," Cal. Bus. & Prof. Code § 17200.

Fraudulent

117. Wal-Mart and Lang's claims that Equate provides "clinical strength," "high absorption," and "3 times better absorption" than competitors, that it generally supports heart health and benefits statin users, and that it is comparable to Qunol, are false and misleading, and fraudulent under the UCL, because Equate is only partially effective, and not comparable to Qunol, as alleged herein. Thus, Equate's label is likely to deceive a reasonable consumer.

118. Wal-Mart and Lang's omissions of material facts are also prohibited by the UCL's "fraudulent" prong.

Unfair

119. Wal-Mart and Lang's conduct with respect to the labeling, advertising, and sale of Equate was unfair because Wal-Mart and Lang's conduct was immoral, unethical, unscrupulous, or substantially injurious to consumers and the utility of its conduct, if any, does not outweigh the gravity of the harm to its victims.

120. Wal-Mart and Lang's conduct with respect to the labeling, advertising, and sale of Equate was also unfair because it violated public policy as declared by specific constitutional, statutory or regulatory provisions, including the False Advertising Law.

121. Wal-Mart and Lang's conduct with respect to the labeling, advertising, and sale of Equate was also unfair because the consumer injury was substantial, not outweighed by benefits to consumers or competition, and not one consumers themselves could reasonably have avoided.

Unlawful

122. The acts alleged herein are "unlawful" under the UCL in that they violate the following laws:

- The Magnuson-Moss Warranty Act, 15 U.S.C. §§ 2103 *et seq.*;
- The Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 *et seq.*;
- The Lanham Act, 15 U.S.C. §§ 1501 *et seq.*;
- The False Advertising Law, Cal. Bus. & Prof. Code §§ 17500 *et seq.*;
- The Consumers Legal Remedies Act, Cal. Civ. Code §§ 1750 *et seq.*; and
- The California Sherman Law, Cal. Health & Safety Code §§ 109875 *et seq.*

* * *

123. In accordance with Cal. Bus. & Prof. Code § 17203, plaintiff seeks an order enjoining Wal-Mart and Lang from continuing to conduct business through unlawful, unfair, or fraudulent acts and practices, and to commence a corrective advertising campaign.

124. On behalf of herself and the subclass, plaintiff also seeks an order for the restitution of all monies from the sale of Equate that were unjustly acquired through acts of unlawful, unfair, or fraudulent competition.

THIRD CAUSE OF ACTION

VIOLATIONS OF THE CALIFORNIA FALSE ADVERTISING LAW, CAL. BUS. & PROF. CODE §§ 17500 *ET SEQ.*

(By the California Subclass Against Wal-Mart and Lang)

125. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

126. The FAL prohibits any statement in connection with the sale of goods "which is untrue or misleading," Cal. Bus. & Prof. Code § 17500.

127. Wal-Mart and Lang's claim that Ultra provides "clinical strength," "high absorption," and "3 times better absorption" than competing products, and that it generally supports heart health and benefits statin users, is untrue or misleading in that Equate does not sufficiently dissolve for effectiveness.

128. Wal-Mart and Lang knew, or reasonably should have known, that the claims were untrue or misleading.

129. Plaintiff and members of the subclass are entitled to injunctive and equitable relief, and restitution in the amount they spent on the Wal-Mart Equate.

FOURTH CAUSE OF ACTION

VIOLATIONS OF THE CALIFORNIA CONSUMERS LEGAL REMEDIES ACT, CAL. CIV. CODE §§ 1750 *ET SEQ.*

(By the California Subclass Against Wal-Mart and Lang)

130. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

131. The CLRA prohibits deceptive practices in connection with the conduct of a business that provides goods, property, or services primarily for personal, family, or household purposes.

132. Wal-Mart and Lang's policies, acts, and practices were designed to, and did, result in the purchase and use of the products primarily for personal, family, or household purposes, and violated and continue to violate the following sections of the CLRA:

a. § 1770(a)(2): misrepresenting the source, sponsorship, approval, or certification of goods or services;

b. § 1770(a)(3): misrepresenting the affiliation, connection, or association with, or certification by, another;

c. § 1770(a)(5): representing that goods have characteristics, uses, or benefits which they do not have;

d. § 1770(a)(6): representing that goods are original or new if they have deteriorated unreasonably or are altered, reconditioned, reclaimed, used, or secondhand;

e. § 1770(a)(7): representing that goods are of a particular standard, quality, or grade if they are of another;

f. § 1770(a)(8): disparaging the goods, services, or business of another by

false or misleading representation of fact;

g. § 1770(a)(9): advertising goods with intent not to sell them as advertised; and

h. § 1770(a)(16): representing the subject of a transaction has been supplied in accordance with a previous representation when it has not.

133. As a result, plaintiff and the subclass members have suffered irreparable harm and are entitled to, as against Wal-Mart only, injunctive relief, restitution, damages, punitive damages, and attorneys' fees. In compliance with Cal. Civ. Code § 1782, on August 23, 2013, plaintiff sent written notice to Wal-Mart of her claims, which both Wal-Mart and its registered agent received on August 26, 2013. A true and correct copy of the letter is attached hereto as Exhibit 13.

134. Plaintiff and the subclass members have suffered irreparable harm and are entitled to, as against Lang, injunctive relief, restitution, and attorneys' fees. Plaintiff does not currently seek damages under the CLRA as against Lang.

FIFTH CAUSE OF ACTION

BREACH OF EXPRESS WARRANTY

(By the Nationwide Class Against Wal-Mart)

135. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

136. In selling Equate to plaintiff and the class members, Wal-Mart made an affirmation of fact or promise that Equate provides "clinical strength," "high absorption," and "3 times better absorption." This affirmation of fact, promise or description formed part of the basis of the bargain. Wal-Mart thus expressly warranted the goods sold.

137. Equate was in the defective condition alleged herein, causing the breach of warranty, when it left Wal-Mart, *i.e.*, when plaintiff and other consumers purchased it. This was the proximate cause of plaintiff's injuries and those of the class.

138. Prior to filing the lawsuit, plaintiff, on behalf of herself and the class, gave Wal-Mart notice of the breach. A true and correct copy of plaintiff's notice letter is attached hereto as Ex. 13.

139. Plaintiff, on behalf of herself and the class, seeks actual damages for Wal-Mart's breach of warranty.

SIXTH CAUSE OF ACTION

BREACH OF IMPLIED WARRANTY OF MERCHANTABILITY

(By the Nationwide Class Against Wal-Mart)

140. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

141. In selling Equate to plaintiff and the class members, Wal-Mart impliedly warranted that the goods sold were merchantable, but laboratory testing demonstrates Equate frequently fails to rupture, providing the consumer with none of the CoQ10 inside. Even when Equate capsules rupture, dissolution may be negligible, less than 2%, giving the consumer virtually no benefit.

142. Plaintiff and the class members suffered injury as a result of Wal-Mart's breach in that they paid money for a product that does not rupture or adequately dissolve, and therefore does not provide the benefits advertised.

143. Prior to filing the lawsuit, plaintiff, on behalf of herself and the class, gave Wal-Mart notice of the breach. A true and correct copy of plaintiff's notice letter is attached hereto as Ex. 13.

144. Plaintiff, on behalf of herself and the class, seeks actual damages for Wal-Mart's breach of warranty.

SEVENTH CAUSE OF ACTION

BREACH OF IMPLIED WARRANTY OF FITNESS

(By the Nationwide Class Against Wal-Mart)

145. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

146. In selling Equate to plaintiff and the class members, Wal-Mart impliedly warranted the goods sold were fit for their particular purpose, e.g., supplementing the body's CoQ10 levels.

147. Wal-Mart breached the warranty. Laboratory testing demonstrates Equate frequently fails to rupture, providing the consumer with none of the CoQ10 inside. Even when Equate capsules rupture, dissolution may be negligible, less than 2%, giving the consumer virtually no benefit.

148. Plaintiff and the class members suffered injury as a result of Wal-Mart's breach in that they paid money for a product that did not adequately rupture or dissolve to be fit for its purpose of supplementing their CoQ10 levels.

149. Prior to filing the lawsuit, plaintiff, on behalf of herself and the class, gave Wal-Mart notice of the breach. A true and correct copy of plaintiff's notice letter is attached hereto as Ex. 13.

150. Plaintiff, on behalf of herself and the class, seeks actual damages for Wal-Mart's breach of warranty.

EIGHTH CAUSE OF ACTION

BREACH OF EXPRESS WARRANTY, CAL. COMM. CODE § 2313

(By the California Subclass Against Wal-Mart)

151. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

152. There was a sale of goods from Wal-Mart to plaintiff and the subclass members.

153. Wal-Mart made an affirmation of fact or promise that Equate provides "clinical strength," "high absorption," and "3 times better absorption." This affirmation of fact, promise or description formed part of the basis of the bargain. Wal-Mart thus expressly warranted the goods sold.

154. Equate was in the defective condition alleged herein, causing the breach of warranty, when it left Wal-Mart, *i.e.*, when plaintiff and other consumers purchased it. This

was the proximate cause of plaintiff's injuries and those of the subclass, who paid money for an ineffective product.

155. Prior to filing this lawsuit, plaintiff, on behalf of herself and the subclass, gave Wal-Mart notice of the breach. A true and correct copy of plaintiff's notice letter is attached hereto as Ex. 13.

156. Plaintiff, on behalf of herself and the subclass, seeks actual damages for Wal-Mart's breach of warranty.

NINTH CAUSE OF ACTION

BREACH OF IMPLIED WARRANTY OF MERCHANTABILITY,

CAL. COMM. CODE § 2313(1)

(By the California Subclass Against Wal-Mart)

157. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

158. "Unless excluded or modified . . . a warranty that goods shall be merchantable is implied in a contract for their sale if the seller is a merchant with respect to goods of that kind." Cal. Comm. Code § 2314(1).

159. There was a sale of goods from Wal-Mart to plaintiff and the subclass members.

160. Wal-Mart impliedly warranted the goods sold were merchantable.

161. In selling Equate to plaintiff and the class members, Wal-Mart impliedly warranted that the goods sold were merchantable, but laboratory testing demonstrates Equate frequently fails to rupture, providing the consumer with none of the CoQ10 inside. Even when Equate capsules rupture, dissolution may be negligible, less than 2%, giving the consumer virtually no benefit.

162. Plaintiff and the class members suffered injury as a result of Wal-Mart's breach in that they paid money for a product that does not rupture or adequately dissolve, and therefore does not provide the benefits advertised.

163. Prior to filing this lawsuit, plaintiff, on behalf of herself and the subclass, gave Wal-Mart notice of the breach. A true and correct copy of plaintiff's notice letter is attached hereto as Ex. 13.

164. Plaintiff, on behalf of herself and the subclass, seeks actual damages for Wal-Mart's breach of warranty.

TENTH CAUSE OF ACTION

BREACH OF IMPLIED WARRANTY OF FITNESS, CAL. COMM. CODE § 2315

(By the California Subclass Against Wal-Mart)

165. Plaintiff realleges and incorporates the allegations elsewhere in the Complaint as if fully set forth herein.

166. "Where the seller at the time of contracting has reason to know any particular purpose for which the goods are required and that the buyer is relying on the seller's skill or judgment to select or furnish suitable goods, there is . . . an implied warranty that the goods shall be fit for such purpose." Cal. Comm. Code § 2315.

167. There was a sale of goods from Wal-Mart to plaintiff and the subclass members.

168. Wal-Mart impliedly warranted the goods sold were fit for their particular purpose, e.g., supplementing the body's natural Coenzyme Q10 production.

169. Wal-Mart breached the warranty. Laboratory testing demonstrates Equate frequently fails to rupture, providing the consumer with none of the CoQ10 inside. Even when Equate capsules rupture, dissolution may be negligible, less than 2%, giving the consumer virtually no benefit.

170. Plaintiff and the class members suffered injury as a result of Wal-Mart's breach in that they paid money for a product that did not adequately rupture or dissolve to be fit for its purpose of supplementing their CoQ10 levels.

171. Prior to filing this lawsuit, plaintiff, on behalf of herself and the subclass, gave Wal-Mart notice of the breach. A true and correct copy of plaintiff's notice letter is attached hereto as Ex. 13.

172. Plaintiff, on behalf of herself and the subclass, seeks actual damages for Wal-Mart's breach of warranty.

PRAYER FOR RELIEF

173. Wherefore, Plaintiff, on behalf of herself, all others similarly situated and the general public, prays for judgment against Wal-Mart and Lang as to each and every cause of action, and the following remedies:

A. An Order certifying this as a class action and appointing plaintiff and her counsel to represent the class and subclass;

B. An Order enjoining Wal-Mart and Lang from labeling, advertising, or packaging Equate with any benefit, efficacy, or comparative claim challenged herein;

C. An Order compelling Wal-Mart and Lang to conduct a corrective advertising campaign to inform the public that Equate did not provide the advertised efficacy or benefits, and was not comparable to Qunol;

D. An Order requiring Wal-Mart and Lang to disgorge or return all monies, revenues, and profits obtained by means of any wrongful or unlawful act or practice;

E. An Order requiring Wal-Mart and Lang to pay all actual and statutory damages permitted under the causes of action alleged herein, if any;

F. An Order requiring Wal-Mart and Lang to pay restitution to restore all funds acquired by means of any act or practice declared by this Court to be an unlawful, unfair, or fraudulent business act or practice, untrue or misleading advertising, or a violation of the UCL, FAL or CLRA, plus pre- and post-judgment interest thereon;

G. Costs, expenses, and reasonable attorneys' fees; and

H. Any other and further relief the Court deems necessary, just, or proper.

JURY DEMAND

174. Plaintiff hereby demands a trial by jury on all issues so triable.

Dated: April 23, 2015

/s/ Jack Fitzgerald

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Attorneys for Plaintiff and the Proposed Classes

Exhibit 1

equate®

CLINICAL STRENGTH

High Absorption

Co Q-10

100 mg

Exhibit 2

Mobile phase, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of impurities in the portion of Ubidecarenone taken:

$$\text{Result} = (r_{T1}/r_{T2}) \times 100$$

r_{T1} = sum of all peak responses, other than that for ubidecarenone

r_{T2} = sum of all peak responses

Acceptance criteria: NMT 1.0%

Procedure 2: Ubidecarenone (2*Z*)-Isomer and Related Impurities

Mobile phase: *n*-Hexane and ethyl acetate (97:3)

System suitability solution: 1 mg/mL of USP Ubidecarenone for System Suitability RS in *n*-hexane

Sample solution: 1 mg/mL of Ubidecarenone in *n*-hexane

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 25-cm; packing L3

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for ubidecarenone (2*Z*)-isomer and ubidecarenone are about 0.85 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the ubidecarenone (2*Z*)-isomer and ubidecarenone

Analysis

Sample: *Sample solution*

Calculate the percentage of impurities in the portion of Ubidecarenone taken:

$$\text{Result} = (r_{T1}/r_{T2}) \times 100$$

r_{T1} = sum of all peak responses, other than that for ubidecarenone

r_{T2} = sum of all peak responses

Acceptance criteria: NMT 1.0%

Total impurities: NMT 1.5%, obtained from *Chromatographic Purity Procedures 1* and *2*

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* ⟨921⟩**:** NMT 0.2%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers.
- **USP REFERENCE STANDARDS** ⟨11⟩

USP Ubidecarenone RS

USP Ubidecarenone Related Compound A RS [coenzyme Q_9]

USP Ubidecarenone for System Suitability RS

Ubidecarenone Capsules

DEFINITION

Ubidecarenone Capsules contain NLT 90.0% and NMT 115.0% of the labeled amount of ubidecarenone ($C_{59}H_{90}O_4$).

IDENTIFICATION

- **A.** The retention time of the major peak of either *Sample solution 1* or *Sample solution 2* corresponds to that of the *Standard solution*, as obtained in the *Procedure* for *Strength*.

STRENGTH

- **PROCEDURE**

[NOTE—Conduct this test promptly with minimum exposure to actinic light.]

Solvent: *n*-Hexane and dehydrated alcohol (5:2)

Mobile phase: Acetonitrile, tetrahydrofuran, and water (55:40:5)

Standard stock solution: 1.0 mg/mL of USP Ubidecarenone RS in *Solvent*

Standard solution: 40 µg/mL in dehydrated alcohol, from the *Standard stock solution*

System suitability stock solution: 1.0 mg/mL of USP Ubidecarenone Related Compound A RS in *Solvent*. Dilute a portion of this solution with dehydrated alcohol to obtain a concentration of 40 µg/mL.

System suitability solution: *Standard solution* and *System suitability stock solution* (1:1)

Sample solution 1 (for soft gelatin Capsules)**:** Open a number of Capsules equivalent to 200 mg of ubidecarenone, quantitatively transfer the shells and contents to a container, add 100 mL of *Solvent*, and shake by mechanical means for 30 min. Using small portions of *Solvent*, quantitatively transfer this mixture to a 200-mL volumetric flask, and dilute with *Solvent* to volume. Centrifuge a portion of this solution, transfer 1.0 mL of the supernatant to a 25-mL volumetric flask, add 2.5 mL of a 0.1% solution of anhydrous ferric chloride in alcohol, and dilute with alcohol to volume.

Sample solution 2 (for hard gelatin Capsules)**:** Empty and thoroughly mix the contents of NLT 20 Capsules. Transfer a portion of the powder, equivalent to 100 mg of ubidecarenone, to a 100-mL volumetric flask, add 60 mL of *Solvent*, and shake by mechanical means for 30 min. Dilute with *Solvent* to volume. Centrifuge a portion of this solution, transfer 1.0 mL of the supernatant to a 25-mL volumetric flask, add 2.5 mL of a 0.1% solution of anhydrous ferric chloride in alcohol, and dilute with alcohol to volume.

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 280 nm

Column: 8-mm × 10-cm; packing L1

Flow rate: 2.5 mL/min

Injection size: 15 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

Suitability requirements

Resolution: NLT 2.5 between ubidecarenone and ubidecarenone related compound A, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0% for ubidecarenone, *Standard solution*

Analysis

Samples: *Sample solution 1* or *Sample solution 2*, and *Standard solution*

Calculate the percentage of the labeled amount of ubidecarenone ($C_{59}H_{90}O_4$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of ubidecarenone from *Sample solution 1* or *Sample solution 2*

r_S = peak area of ubidecarenone from the *Standard solution*

C_S = concentration of USP Ubidecarenone RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of ubidecarenone in *Sample solution 1* or *Sample solution 2* (mg/mL)

Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS

• **DISINTEGRATION AND DISSOLUTION ⟨2040⟩:** Meet the requirements of the test for *Disintegration*, except where the product is labeled to contain a water-soluble form of ubidecarenone. Capsules labeled to contain a water-soluble form of ubidecarenone meet the requirements for the test for *Dissolution*, as follows.

Medium: Water; 500 mL
Apparatus 2: 75 rpm
Time: 60 min
Standard solution: Dissolve 25 mg of USP Ubidecarenone RS in 1 mL of ethyl ether, and dilute with alcohol to obtain a concentration of 2.5 µg/mL. [NOTE—Use a freshly prepared solution only.]
Sample solution: Dilute with alcohol a volume of the solution under test, previously passed through a suitable filter of 0.45-µm pore size, to obtain a concentration of 2.5 µg/mL of ubidecarenone.
Mobile phase and **Chromatographic system:** Proceed as directed in the *Procedure* for *Strength*, except for *Injection size*.
Injection size: 100 µL
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of ubidecarenone ($C_{59}H_{90}O_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S \times V \times D/L) \times 100$$

r_U = peak area of ubidecarenone from the *Sample solution*
r_S = peak area of ubidecarenone from the *Standard solution*
C_S = concentration of USP Ubidecarenone RS in the *Standard solution* (mg/mL)
V = volume of *Medium*, 500 mL
D = dilution factor for the *Sample solution*
L = label claim (mg/Capsule)

Tolerances: NLT 75% of the labeled amount of ubidecarenone ($C_{59}H_{90}O_4$) is dissolved.

SPECIFIC TESTS

• **WEIGHT VARIATION ⟨2091⟩:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
• **LABELING:** Where the product contains a water-soluble form of ubidecarenone, this is so stated on the label.
• **USP REFERENCE STANDARDS ⟨11⟩**
USP Ubidecarenone RS
USP Ubidecarenone Related Compound A RS
Coenzyme Q_9.

Ubidecarenone Tablets

DEFINITION

Ubidecarenone Tablets contain NLT 90.0% and NMT 115.0% of the labeled amount of ubidecarenone ($C_{59}H_{90}O_4$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Procedure* for *Strength*.

STRENGTH

• **PROCEDURE**

[NOTE—Conduct this test promptly with minimum exposure to actinic light.]
Solvent: *n*-Hexane and dehydrated alcohol (5:2)
Mobile phase: Acetonitrile, tetrahydrofuran, and water (11:8:1)
Standard stock solution: 1.0 mg/mL of USP Ubidecarenone RS in *Solvent*
Standard solution: 40 µg/mL from *Standard stock solution* in dehydrated alcohol
System suitability stock solution: 1.0 mg/mL of USP Ubidecarenone Related Compound A RS in *Solvent*. Dilute a portion of this solution with dehydrated alcohol to obtain a concentration of 40 µg/mL.
System suitability solution: *Standard solution* and *System suitability stock solution* (1:1)
Sample stock solution: Weigh and finely powder NLT 20 Tablets. Transfer a quantity of powder, equivalent to about 100 mg of ubidecarenone, to a 100-mL volumetric flask, add 60 mL of *Solvent*, and shake by mechanical means for 30 min. Dilute with *Solvent* to volume, and mix. Centrifuge a portion of this solution, transfer 1.0 mL of the supernatant to a 25-mL volumetric flask, and add 2.5 mL of a 0.1% solution of anhydrous ferric chloride in alcohol. Dilute with alcohol to volume, and mix.
Sample solution: Centrifuge a portion of *Sample stock solution*, transfer 1.0 mL of the supernatant to a 25-mL volumetric flask, add 2.5 mL of a 0.1% solution of anhydrous ferric chloride in alcohol, and dilute with alcohol to volume.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 8-mm × 10-cm; packing L1
Flow rate: 2.5 mL/min
Injection size: 15 µL
System suitability
Samples: *Standard solution* and *System suitability solution*
Suitability requirements
Resolution: NLT 2.5 between ubidecarenone and ubidecarenone related compound A, *System suitability solution*
Tailing factor: NMT 1.5, *Standard solution*
Relative standard deviation: NMT 2.0% for ubidecarenone, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of ubidecarenone ($C_{59}H_{90}O_4$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of ubidecarenone from the *Sample solution*
r_S = peak area of ubidecarenone from the *Standard solution*
C_S = concentration of USP Ubidecarenone RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of ubidecarenone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS

• **DISINTEGRATION AND DISSOLUTION ⟨2040⟩:** Meet the requirements of the test for *Disintegration*, except where the product is labeled to contain a water-soluble form of ubidecarenone. Tablets labeled to contain a water-soluble form of ubidecarenone meet the requirements for the test for *Dissolution*, as follows.

Exhibit 3

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⟨2040⟩ DISINTEGRATION AND DISSOLUTION OF DIETARY SUPPLEMENTS

INTRODUCTION

This general chapter is provided to determine compliance with the disintegration and dissolution standards for dietary supplements where stated in the individual monographs.

For the purposes of this chapter, dietary supplement dosage forms have been divided into three categories: *Vitamin–Mineral Dosage Forms, Botanical Dosage Forms,* and *Dietary Supplements Other Than Vitamin–Mineral and Botanical Dosage Forms. Vitamin–Mineral Dosage Forms* includes articles prepared with vitamins, minerals, or combinations of these dietary ingredients (e.g., USP dietary supplements *Class I* to *Class VI*, described below). *Botanical Dosage Forms* comprises formulations containing ingredients of botanical origin, including plant materials and extracts. *Dietary Supplements Other Than Vitamin–Mineral and Botanical Dosage Forms* encompasses dietary supplements formulated with lawfully recognized dietary ingredients that are different from those pertaining to the two foregoing categories (e.g., amino acids, chondroitin, and glucosamine).

Where a dietary supplement represents a combination of the categories mentioned above, and there is a difference between the requirements for the individual categories, the more stringent requirement applies.

Dissolution testing as described in this chapter is a quality-control tool to enable the performance of dietary supplements to be routinely assessed.

DISINTEGRATION

This test is provided to determine whether dietary supplement tablets or capsules disintegrate within the prescribed time when placed in a liquid medium at the experimental conditions presented below. Compliance with the limits on *Disintegration* stated in the individual monographs for dietary supplements is required except where the label states that the products are intended for use as troches, are to be chewed, or are designed as extended-release dosage forms. Dietary supplements claiming to be extended-release dosage forms must comply with standards other than disintegration to verify that the release of the dietary ingredients from the dosage form is for a defined period of time. Dietary supplements claiming to be extended-release dosage forms shall not be labeled as in compliance with USP unless a USP monograph exists for such product. Determine the type of units under test from the labeling and from observation, and apply the appropriate procedure to 6 or more units.

For purposes of this test, disintegration does not imply complete solution of the unit or even of its active constituent. Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disk, if used, is a soft mass having no palpably firm core.

Apparatus

Apparatus A—Use the *Apparatus* described under *Disintegration* ⟨701⟩ for tablets or capsules that are not greater than 18 mm long. For larger tablets or capsules, use *Apparatus B.*

Apparatus B—The apparatus[1] consists of a basket-rack assembly, a 1000-mL, low-form beaker for the immersion fluid, a thermostatic arrangement for heating the fluid between 35° and 39°, and a device for raising and lowering the basket in the immersion fluid at a constant frequency rate between 29 and 32 cycles per minute through a distance of not less than 53 mm and not more than 57 mm. The volume of the fluid in the vessel is such that at the highest point of the upward stroke the wire mesh remains at least 15 mm below the surface of the fluid and descends to not less than 25 mm from the bottom of the vessel on the downward stroke. At no time should the top of the basket-rack assembly become submerged. The time required for the upward stroke is equal to the time required for the downward stroke, and the change in stroke direction is a smooth transition rather than an abrupt reversal of motion. The basket-rack assembly moves vertically along its axis. There is no appreciable horizontal motion or movement of the axis from the vertical.

Basket-Rack Assembly—The basket-rack assembly consists of three open-ended transparent tubes, each 77.5 ± 2.5 mm long and having an inside diameter of 32.0 to 34.6 mm and a wall 2.0 to 3.0 mm thick; the tubes are held in a vertical position by two plastic plates, each about 97 mm in diameter and 7.5 to 10.5 mm in thickness, with three holes, each about 33 to 34 mm in diameter, equidistant from the center of the plate and equally spaced from one another. Attached to the under surface of the lower plate is 10-mesh No. 23 (0.025-inch) W. and M. gauge woven stainless-steel wire cloth having a plain square weave. The parts of the apparatus are assembled and rigidly held by means of three bolts passing through the two plastic plates. A suitable means is provided to suspend the basket-rack assembly from the raising and lowering device using a point on its axis.

The design of the basket-rack assembly may be varied somewhat provided the specifications for the glass tubes and the screen mesh size are maintained.

Disks—Each tube is provided with a perforated cylindrical disk 15.3 ± 0.15 mm thick and 31.4 ± 0.13 mm in diameter. The disk is made of a suitable, transparent plastic material having a specific gravity of between 1.18 and 1.20. Seven 3.15 ± 0.1-mm holes extend between the ends of the cylinder, one of the holes being through the cylinder axis and the others parallel with it and equally spaced on a 4.2 ± 0.1-mm radius from it. All surfaces of the disk are smooth.[2]

Procedure

Uncoated Tablets—Place 1 tablet in each of the tubes of the basket and, if prescribed, add a disk to each tube. Operate the apparatus, using water or the specified medium as the immersion fluid, maintained at 37 ± 2°. At the end of 30 minutes, lift the basket from the fluid, and observe the tablets: all of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not fewer than 16 of the total of 18 tablets tested disintegrate completely.

Plain Coated Tablets—Place 1 tablet in each of the tubes of the basket and, if the tablet has a soluble external sugar coating, immerse the basket in water at room temperature for 5 minutes. Then, if prescribed, add a disk to each tube, and operate the apparatus, using water or the specified medium as the immersion fluid, maintained at 37 ± 2°. At the end of 30 minutes, lift the basket from the fluid, and observe the tablets: all of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not fewer than 16 of the total of 18 tablets tested disintegrate completely.

Delayed-Release (Enteric-Coated) Tablets—Place 1 tablet in each of the six tubes of the basket, and if the tablet has a soluble external sugar coating, immerse the basket in water at room temperature for 5 minutes. Then operate the apparatus using simulated gastric fluid TS maintained at 37 ± 2° as the immersion fluid. After

[1] An apparatus and disks meeting these specifications are available from Varian Inc., 13000 Weston Parkway, Cary, NC 27513, or from laboratory supply houses.

[2] The use of automatic detection employing modified disks is permitted where the use of disks is specified or allowed. Such disks must comply with the requirements for density and dimensions given in this chapter.

1 hour of operation in simulated gastric fluid TS, lift the basket from the fluid, and observe the tablets: the tablets show no evidence of disintegration, cracking, or softening. Operate the apparatus, using simulated intestinal fluid TS, maintained at 37 ± 2°, as the immersion fluid for the time specified in the monograph. Lift the basket from the fluid, and observe the tablets: all of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

Buccal Tablets—Apply the test for *Uncoated Tablets*. After 4 hours, lift the basket from the fluid, and observe the tablets: all of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

Sublingual Tablets—Apply the test for *Uncoated Tablets*. At the end of the time limit specified in the individual monograph, all of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

Hard Shell Capsules—Apply the test for *Uncoated Tablets,* using as the immersion fluid, maintained at 37 ± 2°, a 0.05 M acetate buffer prepared by mixing 2.99 g of sodium acetate trihydrate and 1.66 mL of glacial acetic acid with water to obtain a 1000-mL solution having a pH of 4.50 ± 0.05. Attach a removable wire cloth, as described under *Basket-Rack Assembly,* to the surface of the upper plate of the basket-rack assembly. At the end of 30 minutes, lift the basket from the fluid, and observe the capsules: all of the capsules disintegrate except for fragments from the capsule shell. If 1 or 2 capsules fail to disintegrate completely, repeat the test on 12 additional capsules: not fewer than 16 of the total of 18 capsules tested disintegrate completely.

Soft Shell Capsules—Proceed as directed under *Rupture Test for Soft Shell Capsules.*

Use of Disks—

VITAMIN–MINERAL DOSAGE FORMS—Add a disk to each tube unless otherwise specified in the individual monograph.

BOTANICAL DOSAGE FORMS—Omit the use of disks unless otherwise specified in the individual monograph.

DIETARY SUPPLEMENTS OTHER THAN VITAMIN–MINERAL AND BOTANICAL DOSAGE FORMS—Omit the use of disks unless otherwise specified in the individual monograph.

NOTE—The use of disks for enteric-coated tablets is not permitted.

RUPTURE TEST FOR SOFT SHELL CAPSULES

Medium: water; 500 mL.

Apparatus—Use *Apparatus 2* as described under *Dissolution* ⟨711⟩, operating at 50 rpm.

Time: 15 minutes.

Procedure—Place 1 capsule in each vessel, and allow the capsule to sink to the bottom of the vessel before starting rotation of the blade. Observe the capsules, and record the time taken for each capsule shell to rupture.

Tolerances—The requirements are met if all of the capsules tested rupture in not more than 15 minutes. If 1 or 2 of the capsules rupture in more than 15 but not more than 30 minutes, repeat the test on 12 additional capsules: not more than 2 of the total of 18 capsules tested rupture in more than 15 but not more than 30 minutes.

Change to read:

DISSOLUTION

This test is provided to determine compliance with the *Dissolution* requirements where stated in the individual monograph for dietary supplements, except where the label states that tablets are to be chewed.

See *Dissolution* ⟨711⟩ for description of apparatus used, *Apparatus Suitability Test,* and other related information. Of the types of apparatus described in ⟨711⟩, use the one specified in the individual monograph.

•Soft gelatin capsule preparations of dietary supplements meet the requirements for *Disintegration.*

Official until May 1, 2010

• (RB 1-May-2009)

For hard or soft gelatin capsules and gelatin-coated tablets that do not conform to the dissolution specification, repeat the test as follows. Where water or a medium with a pH of less than 6.8 is specified as the *Medium* in the individual monograph, the same *Medium* specified may be used with the addition of purified pepsin that results in an activity of 750,000 Units or less per 1000 mL. For media with a pH of 6.8 or greater, pancreatin can be added to produce not more than 1750 USP Units of protease activity per 1000 mL.

This nonspecific dissolution is intended to be diagnostic of known technological problems that may arise as a result of coatings, lubricants, disintegrants, and other substances inherent in the manufacturing process. For dosage forms containing botanical extracts, this dissolution measurement allows an assessment of the extent of decomposition of the extract to polymeric or other nondissoluble compounds that may have been produced by excessive drying or other manipulations involved in the manufacture of botanical extracts. The operative assumption inherent in this procedure is that if the index or marker compound(s) or the extract is demonstrated to have dissolved within the time frame and under conditions specified, the dosage form does not suffer from any of the above formulation or manufacturing related problems.

Vitamin–Mineral Dosage Forms

All dietary supplements belonging to USP *Classes II* to *VI,* prepared as tablets or capsules, are subject to the dissolution test and criteria described in this chapter for folic acid (if present) and for index vitamins and index minerals. This test is required because of the importance of the relationship between folate deficiency and the risk of neural tube defects. The accompanying table lists the dissolution requirements for the individual USP classes of dietary supplements. *Class I* dietary supplements are combinations of oil-soluble vitamins for which dissolution standards are not established; hence, dissolution requirements do not apply to the oil-soluble vitamins contained in formulations belonging to *Class IV* or *Class V.* Vitamin–mineral combinations that may not be strictly covered by USP *Class I* to *Class VI* are subject to the dissolution test and criteria specified in the individual monographs.

Dietary Supplements—Vitamin–Mineral Dosage Forms

USP Class	Combination of Vitamins or Minerals Present	Dissolution Requirement
I	Oil-Soluble Vitamins	not applicable
II	Water-Soluble Vitamins	one index vitamin; folic acid (if present)
III	Water-Soluble Vitamins with Minerals	one index vitamin and one index element; folic acid (if present)
IV	Oil- and Water-Soluble Vitamins	one index water-soluble vitamin; folic acid (if present)
V	Oil- and Water-Soluble Vitamins with Minerals	one index water-soluble vitamin and one index element; folic acid (if present)
VI	Minerals	one index element

Unless otherwise stated in the individual monograph, test 6 dosage units for dissolution as directed under *Dissolution* ⟨711⟩.

DISSOLUTION CONDITIONS FOR FOLIC ACID

NOTE—Perform this test under light conditions that minimize photo degradation.

Medium: water; 900 mL. If the units tested do not meet the requirements for dissolution in water, test 6 additional dosage units for dissolution in a medium of 900 mL of 0.05 M pH 6.0 citrate buffer solution, prepared by mixing 9.5 mL of 0.1 M citric acid monohydrate and 40.5 mL of 0.1 M sodium citrate dihydrate in a 100-mL volumetric flask, diluting with water to volume, mixing, and adjusting to a pH of 6.0 by using either 0.1 M hydrochloric acid or 0.1 M sodium hydroxide solution.

Apparatus 1: 100 rpm, for capsules.

Apparatus 2: 75 rpm, for tablets.

Time: 1 hour.

NOTE—Compliance with the dissolution requirements for folic acid does not exempt the product from dissolution testing of the pertinent index vitamin or the corresponding index mineral.

DISSOLUTION CONDITIONS FOR INDEX VITAMINS AND INDEX MINERALS

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm, for capsules.

Apparatus 2: 75 rpm, for tablets.

Time: 1 hour.

For formulations containing 25 mg or more of the index vitamin, riboflavin, use the following conditions:

Medium: 0.1 N hydrochloric acid; 1800 mL.

Apparatus 1: 100 rpm, for capsules.

Apparatus 2: 75 rpm, for tablets.

Time: 1 hour.

NOTE—Compliance with dissolution requirements for the pertinent index vitamin or index mineral does not exempt the product from dissolution testing of folic acid, if present.

SELECTION OF INDEX VITAMINS AND INDEX ELEMENTS

Compliance with the dissolution requirements for dietary supplements representing combinations of water-soluble vitamins (*Water-Soluble Vitamins Capsules* and *Water-Soluble Vitamins Tablets*) and combinations of oil- and water-soluble vitamins (*Oil- and Water-Soluble Vitamins Capsules* and *Oil- and Water-Soluble Vitamins Tablets*) is determined by measuring the dissolution of a single index vitamin from the water-soluble vitamins present. Riboflavin is the index vitamin when present in the formulation. For formulations that do not contain riboflavin, pyridoxine is the index vitamin. If neither riboflavin nor pyridoxine is present in the formulation, the index vitamin is niacinamide (or niacin), and in the absence of niacinamide (or niacin), the index vitamin is thiamine. If none of the above four water-soluble vitamins is present in the formulation, the index vitamin is ascorbic acid.

Compliance with the dissolution requirements for dietary supplements representing combinations of minerals (*Minerals Capsules* and *Minerals Tablets*) is determined by measuring the dissolution of only one index element. Iron is the index element when present in the formulation. For formulations that do not contain iron, the index element is calcium. If neither iron nor calcium is present, the index element is zinc, and in the absence of all three of these elements, magnesium is the index element.

Compliance with dissolution requirements for dietary supplements representing combinations of water-soluble vitamins and minerals (*Water-Soluble Vitamins with Minerals Capsules* and *Water-Soluble Vitamins with Minerals Tablets*) and combinations of oil- and water-soluble vitamins and minerals (*Oil- and Water-Soluble Vitamins with Minerals Capsules* and *Oil- and Water-Soluble Vitamins with Minerals Tablets*) is determined by measuring the dissolution of one index water-soluble vitamin and one index element, designated according to the respective hierarchies described above.

PROCEDURES

In the following procedures, combine equal volumes of the filtered solutions of the 6 individual specimens withdrawn, and determine the amount of folic acid or the index vitamin or element dissolved, based on the average of 6 units tested. Make any necessary modifications including concentration of the analyte in the volume of test solution taken. Use the *Medium* for preparation of the Standard solution and dilution, if necessary, of the test solution.

Folic Acid—Determine the amount of $C_{19}H_{19}N_7O_6$ dissolved by employing the procedure set forth in the *Assay for folic acid* under *Oil- and Water-Soluble Vitamins with Minerals Tablets*, in comparison with a Standard solution having a known concentration of USP Folic Acid RS in the same *Medium*.

Niacin or Niacinamide, Pyridoxine, Riboflavin, and Thiamine—Determine the amount of the designated index vitamin dissolved by employing the procedure set forth in the *Assay for niacin or niacinamide, pyridoxine, riboflavin, and thiamine* under *Water-Soluble Vitamins Tablets.*

Ascorbic Acid—Determine the amount of $C_6H_8O_6$ dissolved by adding 10 mL of 1.0 N sulfuric acid and 3 mL of starch TS to 100.0 mL of test solution, and titrating immediately with 0.01 N iodine VS. Perform a blank determination, and make any necessary correction.

Iron, Calcium, Magnesium, and Zinc—Determine the amount of the designated index element dissolved by employing the procedure set forth in the appropriate *Assay* under *Minerals Capsules*.

TOLERANCES

The requirements are met if not less than 75% of the labeled content of folic acid and not less than 75% of the labeled content of the index vitamin or the index element from the units tested is dissolved in 1 hour.

Botanical Dosage Forms

Compliance with dissolution requirements necessitates the testing of 6 dosage units individually, or testing 2 or more dosage units in each of the 6 vessels of the dissolution apparatus, and measuring the dissolution of one or more index/marker compound(s) or the extract specified in the individual monograph.

PROCEDURES

Combine equal volumes of the filtered solutions of the 6 or more individual specimens withdrawn, and use the pooled sample as the test solution. Determine the average amount of index or marker compound(s) or the extract dissolved in the pooled sample by the *Procedure* specified in the individual monograph. Make any necessary modifications, including concentration of the analyte in the volume of the test solution taken. Use the *Medium* for preparation of the Standard solution and dilution, if necessary, of the test solution.

INTERPRETATION

Pooled Sample—Unless otherwise specified in the individual monograph, the requirements are met if the quantities of the index or marker compound(s) or the extract dissolved from the pooled sample conform to the accompanying acceptance table. The quantity, Q, is the amount of dissolved index or marker compound(s) or the extract specified in the individual monograph, expressed as a percentage of the labeled content. The 5%, 15%, and 25% values in the acceptance table are percentages of the labeled content so that these values and Q are in the same terms.

Acceptance Table for a Pooled Sample

Stage	Number Tested	Acceptance Criteria
S_1	6	Average amount dissolved is not less than Q + 10%
S_2	6	Average amount dissolved (S_1 + S_2) is equal to or greater than Q + 5%
S_3	12	Average amount dissolved (S_1 + S_2 + S_3) is equal to or greater than Q

Dietary Supplements Other Than Vitamin–Mineral and Botanical Dosage Forms

Unless otherwise stated in the individual monographs for dietary supplement dosage forms in this category, compliance requires the testing of 6 individual units, measuring the dissolution of the dietary ingredient as the average of the 6 units tested.

PROCEDURES

Combine equal volumes of the filtered solutions of the 6 specimens withdrawn, and use the pooled sample as the test solution. Determine the average amount of dietary ingredient dissolved in the pooled sample by the *Procedure* specified in the individual monograph. Make any necessary modifications, including concentration of the analyte in the volume of the test solution taken. Use the *Medium* for preparation of the Standard solution and for dilution, if necessary, of the test solution.

TOLERANCES

Because of the diversity of chemical characteristics and solubilities of dietary ingredients pertaining to this category, general tolerances cannot be established. See individual monographs for *Tolerances*.

Exhibit 4

US008158134B1

(12) **United States Patent**
Supersaxo et al.

(10) **Patent No.: US 8,158,134 B1**
(45) **Date of Patent: Apr. 17, 2012**

(54) **MICROEMULSION PRECONCENTRATE, MICROEMULSION AND USE THEREOF**

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(58) **Field of Classification Search** 424/439, 424/466, 401; 510/407, 421
See application file for complete search history.

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(57) **ABSTRACT**

The invention relates to compositions in the form of microemulsion preconcentrates that contain (a) a mixture that consists of a medium-chain triglyceride and an omega-9 fatty acid and/or an omega-6 fatty acid; and (b) a surface-active component that contains a polyoxethylene tenside. When contacted with water or with an aqueous medium these microemulsion preconcentrates form microemulsions. The microemulsions of the O/W type have an average particle size below 150 nm, preferably below 100 nm. The inventive microemulsion preconcentrates and microemulsions are suitable for use as vehicles for substances, namely active agents, that are hardly soluble in water, but soluble in components (a) and/or (b). In the aqueous phase, said microemulsions may contain water-soluble substances.

22 Claims, No Drawings

Exhibit 5

Microemulsion-preconcentrates and microemulsions comprising coenzyme Q10

EP 1249230 B1

IMAGES (1)

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Inventors	Andreas Werner Supersaxo, Hans Georg Weder, Marc Antoine Weder
Applicant	Vesifact Ag
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DESCRIPTION translated from German

[0001] The present invention relates to novel formulations in the form of microemulsion preconcentrates and microemulsions, and to their use as a carrier system for poorly soluble active ingredients in water, from the class of ubiquinones, optionally also in combination with vitamins and trace elements. The formulations of the invention are particularly suitable for oral administration in the form of unit dosage forms.

[0002] Ubiquinones can be detected in almost all organisms in large quantities, the only exceptions are Gram-positive and cyanobacteria. Ubiquinones are depending on the number in the side chain of linked isoprene units as Q1, Q2, Q3, etc. referred. They occur preferentially with specific chain lengths, for example in some micro-organisms and yeasts with n = 6 in most mammals, including humans, to outweigh the coenzyme Q10, also known as ubidecarenone. The human body synthesizes some of its coenzyme Q10-demand, and the rest is absorbed by the food. With increasing age, the endogenous production of coenzyme Q10 decreases continuously.

[0003] The multiple effects of coenzyme Q10 are based both on its biological functions in energy metabolism of the cells as well as its antioxidant properties. Due to these effects Coenzyme Q10 is used for the prophylaxis and / or treatment of the following diseases:

Heart and circulatory diseases such as heart attack, angina, atherosclerosis and hypertension
Degenerative diseases of the central nervous system such as Alzheimer's, Parkinson's and depression,
Gum disease
Muscular dystrophy
Male infertility,
boosting the immune system and

to improve exercise capacity. Further, coenzyme Q10 prevent or reduce side effects of certain drugs, or, for example. Those statins such as lovastatin, pravastatin and simvastatin or cytostatic agents such as doxorubicin

[0004] Coenzyme Q10 is a lipophilic (ie hydrophobic) substance with very low solubility in water (practically insoluble). Formulations of Coenzyme Q10, for example, for oral administration are based on the application, therefore, mainly of oils or similar excipients as carrier media. The thus formulated and currently commercially available, preparations for oral administration such as Super Bio-Quinone (Pharma Nord), Bio Coenzyme Q10 (Solanova) and Q-Gel Ultra (Tishcon) have a very low bioavailability.

[0005]

CLAIMS (21)

1. A composition in the form of a microemulsion preconcentrate containing

(a) a mixture comprising a triglyceride and an omega-9-fatty acid and/or an omega-6-fatty acid; and

(b) a surface-active component containing a tenside, in particular of polyoxyethylene type, and

(c) an active substance mixture containing a ubiquinone, preferably Q10, in combination with vitamins, preferably vitamin E and derivatives thereof, and/or trace elements, wherein the ubiquinone is soluble in (a) and/or (b).

2. A composition in the form of a microemulsion which can be obtained by mixing a microemulsion preconcentrate according to claim 1 with water or an aqueous medium.

3. A composition according to claim 1 or claim 2 which is substantially free of components which are miscible with water or soluble in water.

4. A composition according to one of claims 1 to 3 **characterised in that** the fatty acid residues of the triglyceride have 4-18, preferably 6-18 C-atoms.

5. A composition according to claim 4 **characterised in that** the triglyceride is a caprylic/capric acid triglyceride.

6. A composition according to one of claims 1 to 5 **characterised in that** the omega-9-fatty acid and/or the omega-6-fatty acid has 12-14, in particular 16-24, preferably 18-22 C-atoms.

7. A composition according to one of claims 1 to 6 **characterised in that** the omega-9-fatty acid is oleic acid.

8. A composition according to claim 6 or claim 7 **characterised in that** the omega-6-fatty acid is linoleic acid.

9. A composition according to one of claims 1 to 8 **characterised in that** as component (a) it contains a mixture of a caprylic/capric acid triglyceride, oleic acid and/or linoleic acid.

10. A composition according to one of claims 1 to 9 **characterised in that** the quantitative ratio of omega-9-fatty acid and/or omega-6-fatty acid to the glyceride is 1:1 to 1:200, preferably

Kommuru et al. (Int. J. Pharm 212 (2001): 233-246) describe self-emulsifiable systems for administration of coenzyme Q10.

Object of the present invention is to develop a formulation which improves the bioavailability of coenzyme Q10. It has surprisingly been found that when a dosage of formulations based on a microemulsion preconcentrate the oral bioavailability of coenzyme Q10 as compared with the above-mentioned commercially available compounds is significantly higher.

Under the inventive microemulsion preconcentrate a system is understood as follows upon contact with water or other aqueous medium, such as simulated gastric or intestinal juice, for example, when added to water, a microemulsion. In such a microemulsion, it is conventionally accepted sense in a non-opaque or substantially non-opaque colloidal dispersion comprising water and containing organic components, including lipophilic (ie, hydrophobic) components.

Microemulsions according to the invention can be identified by the fact that they have one or more of the following properties:

They are formed spontaneously when their components are brought into contact, so it is this virtually no supply of energy is necessary, and the formation of such microemulsions is therefore without heating or application of a high shearing force or any other substantially mixing.

They are virtually non-opaque, that is transparent or opalescent when viewed under an optical microscope. They are in their undisturbed state, optically isotropic, although at an observation example, using an X-ray technology can determine an anisotropic structure.

They contain a dispersed or particulate (droplet) phase, the particles have a size of less than 200 nm, which originates their optical transparency. The particles may be spherical or have other structures, for example, they may be liquid crystals with lamellar, hexagonal or isotropic symmetry. Generally microemulsions comprise droplets or particles having a maximum dimension, for example, a diameter of less than 150 nm, usually about 10-100 nm

In the inventive microemulsion preconcentrates are accordingly to galenic systems containing a poorly water-soluble therapeutic agent from the class of ubiquinones and when brought into contact with water or

Gastric and intestinal fluids are spontaneously or substantially spontaneously, ie without enabling significant energy input to form a microemulsion.

The invention provides a composition in the form of a microemulsion preconcentrate is containing

(A) a mixture consisting of a triglyceride and an omega-9 fatty acid and / or an omega-6 fatty acid, and

(B) a surfactant component comprising a surfactant, in particular of polyoxyethylene type,

(C) an active substance mixture containing a ubiquinone, preferably Q10,. In combination with vitamins, preferably vitamin E and derivatives thereof, and / or trace elements, wherein the ubiquinone in (a) and / or (b) is releasably

- The invention relates to effervescent tablets and granules and containing a composition in the form of a microemulsion preconcentrate containing
- (A) a mixture consisting of a triglyceride and an omega-9 fatty acid and / or an omega-6 fatty acid, and
- (B) a surfactant component comprising a surfactant, in particular of polyoxyethylene type,
- (C) an active ingredient selected from the class of ubiquinones, wherein the active agent in (a) and / or (b) is soluble.
- The inventive microemulsion preconcentrates are preferably characterized in that they
- (A), a mixture consisting of a medium chain triglyceride and an omega-9 fatty acid and / or an omega-6 fatty acid
- (B) a surfactant component comprising a surfactant include polyoxyethylene type and
- (C) a sparingly water-soluble, in component (a) and / or (b), however, soluble therapeutic agent from the class of ubiquinones included.
- The ratio of the components (a): (b): (c), (a): (c) or (b): (c) of the novel microemulsion must be chosen, of course, so that the active compound (c) is solubilized stable ie it may not occur for several weeks precipitates.

1:2 to 1:20.

11. A composition according to one of claims 1 to 10 **characterised in that** the surface-active component (b) is a polyoxyethylene sorbitan fatty acid ester, a polyoxyethylene-glycolated natural or hydrated vegetable oil or mixtures thereof.

12. A composition according to one of claims 1 and 3 to 11 **characterised in that** the component (a) is present in an amount of 20 to 70 percent by weight with respect to the total weight of the composition.

13. A composition according to one of claims 1 and 3 to 12 **characterised in that** the surface-active component (b) is present in an amount of 20 to 80 percent by weight with respect to the total weight of the composition.

14. A composition according to one of claims 2 to 13 **characterised in that** it is an O/W-microemulsion with an average particle size of less than 150 nm, preferably less than 100 nm.

15. A shaped body for oral administration containing a composition according to one of claims 1 and 3 to 13 for administering the active substance.

16. , A shaped body according to claim 15 **characterised in that** it contains a biopolymer, in particular gelatin.

17. An effervescent tablet containing a composition according to one of claims 1 and 3 to 13 for administering the active substance.

18. A granular material containing a composition according to one of claims 1 and 3 to 13 for administering the active substance.

19. An effervescent tablet containing a composition in the form of a microemulsion preconcentrate containing

(a) a mixture comprising a triglyceride and an omega-9-fatty acid and/or an omega-6-fatty acid; and

(b) a surface-active component containing a tenside, in particular of polyoxyethylene type, and

(c) an active substance selected from the class of ubiquinones, wherein the active substance is soluble in (a) and/or (b).

20. A granular material containing a composition in the form of a microemulsion preconcentrate containing

(a) a mixture comprising a triglyceride and an omega-9-fatty acid and/or an omega-6-fatty acid; and

(b) a surface-active component containing a tenside, in particular of polyoxyethylene type, and

(c) an active substance selected from the class of ubiquinones, wherein the active substance is soluble in (a) and/or (b).

21. Use of a shaped body, granular material or effervescent tablet according to one of claims 15 to 20 which break down in the gastrointestinal tract, for producing a medicament for release of a composition spontaneously forming a microemulsion with gastrointestinal juice.

- In contrast to the formulations of the prior art, the microemulsion preconcentrates of the present invention is substantially free of components with water-miscible or soluble in water. This is in particular the components
    - $C_{1-C\ 5}$ alkyl or tetrahydrofurfuryl diethers or partial ethers of low molecular weight mono-or polyoxy-$C_{2-C\ 12}$ alkanediols;
    - 1,2-propylene glycol;
    - lower alkanols;
    - Esterification products of polycarboxylic acids with 2-10, especially 3-5 carboxyl groups with $C_{1-C\ 10}$ alcohols, and
    - Esterification products of polyols with 2-10, especially 3-5 carboxyl groups with $C_{2-C\ 11\text{-carboxylic}}$ acids;

  in particular substantially free from diethylene glycol monomethyl ether, glycofurol, 1,2-propylene glycol, triethyl citrate, Tributycitrat, Acetyltributycitrat, acetyl citrate, triacetin, ethanol, polyethylene glycol, and propylene carbonate dimethylisosorbitol.
- In contrast to the relevant formulations according to WO 98/40051 A component (a) of the inventive microemulsion preconcentrate, in addition to a medium chain triglyceride, an omega-9 fatty acid and / or an omega-6 fatty acid, which surprisingly have a particularly pronounced stability novel microemulsions is connected, which is for their therapeutic usefulness is crucial.
- The inventive microemulsion preconcentrates may be prepared by mixing the individual components, optionally with heating, intimately mixed together. The microemulsion preconcentrates may also be prepared by dissolving the component (b), with stirring, optionally under heating, in the component (a), and the resulting solution was added with further stirring with the component (c). Here, it is of particular importance in that the component or the active ingredient (c) in either component (a) or component (b) or in both components (a) and (b) is releasable and that the manufacture of the pre-concentrate, ie the mixture of all three components (a), (b) and (c) the active substance is present in any case remain in dissolved form.
- As component (a) mixtures are of a medium chain fatty acid, advantageously a fatty acid triglyceride in which the fatty acid residues 4 to 18, preferably 6 to 18 carbon atoms, and an omega-9 and / or an omega-6 fatty acid. These substances are not miscible with water and insoluble in water and practically insoluble and have no or virtually no surfactant function.
- Preferred medium chain fatty acid triglycerides are Capryl-/Caprinsäure-Triglyceride as they are available, for example under the trade name MIGLYOL known and commercially (Fiedler, Lexikon der excipients, 3rd Edition, pages 808-809, 1989). They include the following products:
  MIGLYOL 810, 812 and 818
- It is a fractionated coconut oil which contains triglycerides of caprylic and capric acid, and a molecular weight of about 520 (MIGLYOL 810 and 812) and 510 has (MIGLYOL 818). It has a fatty acid composition of C_6 of maximum 2 percent (MIGLYOL 810) and 3 percent (MIGLYOL 812 and 818), with C_8 from about 65 to 75 percent (MIGLYOL 810), 50 to 65 percent (MIGLYOL 812) and 45 to 60 percent (MIGLYOL 818). C_{10} is at 25 to 35 percent with MIGLYOL in MIGLYOL 812 with about 30 to 45 percent, and MIGLYOL 818 represented about 25 to 40 percent C_{12} with a maximum of 2 percent (MIGLYOL 810), 5 percent (MIGLYOL 812), and 2 to 5 percent (MIGLYOL 818). MIGLYOL 818 additionally has a content of $C_{18:2}$ of about 4 to 6 percent.
- Further, triglycerides of caprylic and capric acids are suitable, as they are known under the trade name MYRITOL and are available (Fiedler, Lexikon der excipients, 3rd Edition, page 834, 1989). These include for example the product 813th MYRITOL
- Other suitable products of this class are CAPTEX 355, CAPTEX 300, CAPTEX 800, CAPMUL MCT, NEOBEE M5 and Mazol 1400th
- Suitable omega-9 fatty acids are mainly those having 12-24, in particular 16-24, preferably 18-22 carbon atoms, such as oleic acid and eicosatrienoic. Particularly preferred is the oleic acid.
- Suitable omega-6 fatty acids are mainly those with 12-24, in particular 16-24, preferably 18-22 carbon atoms, for example, linoleic acid, gamma-linolenic acid, dihommo-gamma-linolenic acid and arachidonic acid. Particularly preferred is the linoleic acid.
- In a particularly preferred embodiment is used as the component (a) a mixture consisting of one Capryl-/Caprinsäure-Triglycerid, oleic acid and / or linoleic acid.
- Component (c), which are sparingly soluble in water, in the component (a) and / or (b), however, soluble therapeutic agent from the class of ubiquinones, preferably coenzyme Q10, though it may also be another suitable ubiquinone, optionally in combination with vitamins , preferably vitamin E, and / or trace elements may be used.
- Wherein component (b), the surface-active component containing a tenside of polyoxyethylene type, it may be a hydrophilic surfactant or a lipophilic surfactant, but also mixtures of such agents come into question.
- Examples of such surfactants are as follows:
    - Reaction products of natural or hydrogenated vegetable oils and ethylene glycol, namely polyoxyethylene glycolated natural or hydrogenated vegetable oils such as polyoxyethylene glycolated natural or hydrogenated castor oils. Especially useful are the various surfactants known as Cremophor and are available (Fiedler, Lexikon der excipients, 3rd edition, pages 326 to 327, 1989), especially those products with the names Cremophor RH 40, Cremophor RH 60 and Cremophor EL. Also suitable for use as such products, the various surfactants sold under the name NIKKOL known and available, for example, NIKKOL HCO-60.
    - Polyoxyethylene, such as the mono-and Trilaurylester, the mono-and Tripalmitylester, the mono-and Tristearylester and the mono-and Trioleylester as under the name TWEEN are known and available (Fiedler, Lexikon der excipients, 3rd Edition, pages 1300 to 1304, 1989), for example, the products
      Tween 20: polyoxyethylene (20) sorbitan,
      TWEEN 40: polyoxyethylene sorbitan monopalmitate (20)
      TWEEN 60: polyoxyethylene sorbitan monostearate (20)
      TWEEN 80: Polyoxyethylene sorbitan monooleate (20),
      TWEEN 65: polyoxyethylene sorbitan (20),
      TWEEN 85: polyoxyethylene (20) sorbitan,
      TWEEN 21: Polyoxyethylene sorbitan monolaurate (4),
      TWEEN 61: polyoxyethylene sorbitan monostearate (4) and
      TWEEN 81: Polyoxyethylene sorbitan monooleate (4).

- Particularly preferred from this class of compounds is TWEEN 80
    - Polyoxyethylene fatty acid esters, such as those commercially available under the name MYRJ known and available Polyoxyethylenstearinsäureester (Fiedler, Lexikon der excipients, 3rd Edition, page 834, 1989), especially the product MYRJ 52, and also under the name CETIOL HE known and available polyoxyethylene (Fiedler Encyclopedia of excipients, 3rd edition, page 284, 1989).
    - Copolymers of polyoxyethylene and polyoxypropylene like. Example, under the names Pluronic and EM Kalyx are known and available (Fiedler, Lexikon der excipients, 3rd Edition, pages 956-958, 1989), especially the product Pluronic F68
    - Block copolymers of polyoxyethylene and polyoxypropylene, as for example under the name POLOXAMER are known and available (Fiedler, Lexikon der excipients, 3rd Edition, page 959, 1989), especially the product POLOXAMER 188th
    - Polyethoxylated vitamin E derivatives, in particular the product Vitamin E TPGS (d-alpha Tocoperyl Polyethylene Glycol 1000 Succinate, Eastman).
    - Polyethoxylated hydroxyfatty, especially the product Solutol HS 15 (polyoxyethylene-660-hydroxystearate, BASF).
    - Transesterification of natural Pflanzenölglyceriden and Polyethylenpolyolen. These include transesterification of different, for example, non-hydrogenated, vegetable oils such as corn oil, pumpkin seed oil, almond oil, peanut oil, olive oil and palm oil, and mixtures thereof with polyethylene glycols, in particular those which have an average molecular weight of 200-800. Several such transesterification are known as LABRAFIL known and available (Fiedler, Lexikon der excipients, 3rd edition, page 707, 1989), of which the products Labrafil M 1944 CS and Labrafil M 2130 CS particularly suitable.

- Ethylene oxide adducts of sterols and derivatives thereof, thereof, for example, cholesterol and derivatives, such as products which are derived from sitosterol, campesterol or stigmasterol, for example Sojasterolen and derivatives thereof (Fiedler, Lexikon der Hilfsstoffe, 3rd edition, pages 554 and 555, 1989), as they are known and are available under the designations Generol, are in particular the products Generol 122 E5, 122 E10, and 122 E25.
- The inventive microemulsion preconcentrates comprise both systems which contain a single surfactant, as well as systems that contain a mixture of two or more surfactants, eg Tween 80 + CREMOPHOR RH 40, TWEEN 80 + CREMOPHOR RH 40 + VITAMIN E TPGS etc .
- According to the invention is preferably used, a surface-active component containing a polyoxyethylene, a polyoxyethylene glycolated natural or hydrogenated vegetable oil or mixtures thereof.
- The inventive microemulsion preconcentrates may also contain other substances, such as antioxidants, thickeners, fragrances and / or flavoring agents, coloring agents, etc.
- The inventive pre-microemulsions are primarily intended for oral use. Preference is given the so-called A unit dosage form, ie, the microemulsion preconcentrate is in a molded body such as a soft or hard capsule as spent from gelatin or starch. Containing the active ingredient if the pre-microemulsion is released forms spontaneously in conjunction with gastrointestinal fluid, a microemulsion. Compositions of the invention prove to be suitable for oral administration in the form of Einheitsdosisformem also therefore be particularly suitable, because the addition of volatile organic solvents, in particular from ethanol commonly used is not required. The use of the said solvents is adversely affected by its evaporation through the outer wall of the shaped body, in particular of soft or hard gelatin capsule, the storability and the active ingredient crystallizes. The occurrence of these adverse effects should be avoided by expensive measures in packing and storage.
- The new compositions can also be processed into effervescent tablets or granules.
- A unit dosage form of the above-described type contains advantageously 0.5 to 25, preferably 10-20 weight percent of a sparingly soluble in water, in the component (a) and / or (b), however, soluble therapeutic agent of the class of ubiquinones (component (c)), 9.5 to 70, preferably 20 to 70 weight percent and more preferably 25 to 65 weight percent of a mixture consisting of a medium chain triglyceride and an omega-9 fatty acid and / or an omega-6 fatty acid (component (a)) and 20 to 90, preferably 25 to 65 weight percent of the surface-active component (b).
- By the present invention can also be pharmaceutical compositions provide, the sparingly soluble one in water, present in component (a), but soluble therapeutic agent from the class of ubiquinones and representing itself microemulsions; these microemulsions is the active ingredient solubilized stable with several weeks, no precipitates are observed. For oral administration may be microemulsions, obtained for example by diluting the inventive microemulsion preconcentrates with water or an aqueous medium, can be directly used as drinking formulations. Is a parenteral application is provided, then include compositions in which other excipients may be present, also water, so that an aqueous microemulsion in the form of an injection solution, an infusion solution or the like is obtained.
- Such pharmaceutical compositions in the form of microemulsions are also new and object of the present invention.
- The novel micro-emulsions can be produced from the novel microemulsion preconcentrates by dilution with water or other aqueous liquids. When contacting the pre-concentrate with water or stomach and intestinal juice is spontaneously or substantially spontaneously, ie without significant energy input a microemulsion formed.
- Depending on the amount of water present is W / O microemulsions, to bicontinuous microemulsions or O / W microemulsions.
- The novel microemulsions of the O / W type (oil-in-water) exhibit stability properties, such as they have been described above in connection with micro-emulsions, that is, in particular, that in these microemulsions of the active agent is solubilized stable over several weeks no precipitate can be observed. The particle size of these microemulsions is less than 150 nm, preferably less than 100 nm by the following examples compositions of the invention are explained further. Examples 1.1 to 3.1 show the preparation of compositions in oral unit dosage forms of, for example, for the prevention or treatment of heart and circulatory diseases, degenerative diseases of the central nervous system, gum disease, muscular dystrophy, male infertility, to strengthen the immune system, improve physical performance and for preventing or reducing side effects of statin-induced suitable. Example 2.1 demonstrates the preparation of a composition for parenteral application. In Example 3, the oral bioavailability of a composition of the invention is determined and compared with those of commercially available compounds.
- The examples are described with particular reference to coenzyme Q10. Using other appropriate Ubiquinone, optionally in combination with vitamins, preferably vitamin E and / or trace elements may be produced, however, similar compositions.

Example 1: Preparation of oral coenzyme Q10 dosage forms of the type microemulsion preconcentrate Example 1.1

- Coenzyme Q10 (c1) 10.00%
  Miglyol 812 (a1) 38.90%
  Oleic acid (a2) 6.00%
  Tween 80 (b) 45.00%
  Vitamin E (c2) 0.10%

  The coenzyme Q10 (c1) is introduced with stirring at 40 - 45 ° C dissolved in the components (a1), (a2), (b) and (c2). The formed microemulsion preconcentrate is filled into a soft or hard gelatin capsule or made into effervescent tablets.
- Alternatively, the microemulsion preconcentrate also be filled into a dispenser. In this case the patient is by appropriate dilution with water or another aqueous liquid from the microemulsion preconcentrate forth an oral drink solution of the type O / W microemulsion.
- In a similar manner can also be prepared the following compositions.

Reference Example 1.2

- Coenzyme Q10 (c) 10.00%
  Miglyol 812 (a1) 35.00%
  Oleic acid (a2) 10.00%
  Tween 80 (b1) 33.75%
  Cremophor EL (b2) 11.25%

Reference Example 1.3

- Coenzyme Q10 (c) 20.00%
  Miglyol 812 (a1) 25.00%
  Oleic acid (a2) 10.00%
  Tween 80 (b1) 33.75%
  Cremophor EL (b2) 11.25%
- Compositions of the above type can be diluted with water, for example at 1:10, arise microemulsions, the following particle sizes have (see Table 1):

Composition microemulsion preconcentrate O / w microemulsion

	Particle diameter [Nm]	Standard deviation [1] [nm]
Example 1.1	35.7	2.14
Example 1.2	6.26	9.8
Example 1.3	28.0	6.10

- The table below shows that the microemulsion formation of microemulsion preconcentrates unchanged after filling and storage in soft gelatin capsules (WHC) remains.

Microemulsion preconcentrate Example 1.1	Particle diameter of the coenzyme Q10 microemulsion	
	Gastric juice [nm]	Intestinal juice [nm]
Before filling in WHC	41.9 ± 18.1	39.0 ± 16.1

After filling in WHC	41.5 ± 18.9	37.8 ± 19.5
After 1 month of storage narrowing in WHC at 25 ° C and 60% RH	45.2 ± 17.9	40.6 ± 16.8
After 1 month of storage narrowing in WHC at 40 ° C and 75% RH	44.9 ± 20.2	39.5 ± 17.3
After 3-month storage narrowing in WHC at 25 ° C and 60% RH	43.0 ± 17.6	39.4 ± 17.1

Example 2: Preparation parenterally applicable CoQ10 forms of type microemulsion

- The described in Example 1.1 to 1.3 microemulsion preconcentrates can serve as the basis for the production of injection or infusion solutions by being with other additives, such as normal saline or 5% glucose solution and the like, diluted accordingly.
- Example 2.1: Coenzyme Q10 0.10% infusion
  Microemulsion preconcentrate according to Example 1.2 1.00%
  5% glucose solution to 100.00%
- The liquid microemulsion preconcentrate is added under stirring at room temperature of the glucose solution. The resulting coenzyme Q10 O / W microemulsion is 0.2 micron sterile filtered and filled into sterile containers common.

Example 3: bioavailability of coenzyme Q10 microemulsion preconcentrate according to Example 1.1 commercially after oral administration in soft gelatin capsule, compared with three available preparations

- The aim of this four-arm, double-blind, randomized study of 20 subjects of both sexes was to examine the plasma concentration of CoQ10 after a single oral dose of 120 mg. Given intermittently for 24 hours blood samples were taken.

Preparations

- A
  Soft gelatin capsules containing coenzyme Q10
  Microemulsion preconcentrate according to Example 1.1
  Lot 201004
  Active ingredient: 30 mg CoQ10 per capsule

B
  Q-Gel Ultra (Tishcon)
  Batch 19710060
  Active ingredient: 60 mg CoQ10 per capsule

C
  Super Bio-Quinone (Pharma Nord)
  Lot 000956
  Active ingredient: 30 mg CoQ10 per capsule

D
  Bio Coenzyme Q10 (Solanova)
  Batch 00310050
  Active ingredient: 30 mg CoQ10 per capsule

Dosage

- Coenzyme Q10 120 mg orally in 2 or 4 capsules

Taking

- The oral intake of 120 mg Coenmzym Q10 was sober, the morning before breakfast

Volunteers

- n = 20 in 4 groups of 5 subjects (A - D)

Measurement parameters

- Plasma levels of coenzyme Q10 [ug / ml plasma]

Analysis of plasma samples

- The quantitative determination of coenzyme Q10 (ubidecarenone) using HPLC

Devices	HPLC unit MERCK / HITACHI, UV detection, autosamplers F. Beckmann (Spectra Physics)
Column	Nucleosil RP 18 (5µm), 15 cm long, 4 mm diameter, Merck
Eluent	Acetonitrile
Injection loops	100/20 mu.l
UV detector	275 nm
Retention time	10 min
Detection limit	80 ng / ml

Results

- The plasma levels of the compounds A - D show significant differences in terms of reaching the maximum and the permeation rate (see Figure 1). The calculation of the AUC and the derived relative dose available, based on 120 mg single dose, can be significant differences in the bioavailability of coenzyme Q10 after a single oral administration clearly describe. Composition of the invention (test preparation A) is compared to the test specimens B, C and D is a 3-5 fold higher bioavailability (Vg Table 3).

Test preparation	A	B	C	D
AUC [µg/ml/10h]	30.16	5.72	5.14	10.65
Relative available dose based on 120 mg single dose	75.39	14:30	12.86	26.63

CLASSIFICATIONS

International Classification	A61K9/107, A61K31/122, A61K9/48
Cooperative Classification	A61K9/1075, A61K31/122, A61K9/4858
European Classification	A61K9/107D, A61K31/122

LEGAL EVENTS

Date	Code	Event	Description
Aug 30, 2013	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** FR **Payment date:** 20130625

Date	Code	Event	Description
			Payment date: 20130423 **Ref country code:** IT **Ref country code:** FI **Payment date:** 20130410 **Year of fee payment:** 13 **Ref country code:** NL **Ref country code:** PT **Payment date:** 20130405
Jul 31, 2013	PGFP	Postgrant: annual fees paid to national office	**Payment date:** 20130415 **Ref country code:** BE **Ref country code:** CH **Payment date:** 20130627 **Ref country code:** DE **Year of fee payment:** 13 **Payment date:** 20130508 **Ref country code:** GB **Ref country code:** SE **Payment date:** 20130412 **Payment date:** 20130410 **Ref country code:** IE **Ref country code:** DK
May 31, 2013	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** GR **Payment date:** 20130329 **Year of fee payment:** 13
Mar 29, 2013	PGFP	Postgrant: annual fees paid to national office	**Payment date:** 20120327 **Ref country code:** AT **Year of fee payment:** 12
Jan 31, 2013	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** PT **Year of fee payment:** 12 **Payment date:** 20120411
Dec 31, 2012	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** ES **Year of fee payment:** 12 **Payment date:** 20120510
Sep 28, 2012	PGFP	Postgrant: annual fees paid to national office	**Payment date:** 20120420 **Ref country code:** IT **Year of fee payment:** 12
Aug 31, 2012	PGFP	Postgrant: annual fees paid to national office	**Year of fee payment:** 12 **Ref country code:** FI **Ref country code:** SE **Payment date:** 20120411 **Ref country code:** GB **Ref country code:** FR **Payment date:** 20120504
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Sep 30, 2011	PGFP	Postgrant: annual fees paid to national office	**Payment date:** 20110415 **Year of fee payment:** 11 **Ref country code:** IT

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Nov 30, 2010	PGFP	Postgrant: annual fees paid to national office	**Payment date:** 20100409 **Ref country code:** SE **Year of fee payment:** 10
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Aug 31, 2010	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** AT **Payment date:** 20100413 **Ref country code:** DE **Payment date:** 20100430 **Ref country code:** IT **Payment date:** 20100417 **Year of fee payment:** 10 **Ref country code:** NL **Payment date:** 20100402 **Year of fee payment:** 10
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Feb 27, 2009	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** GR **Payment date:** 20080313 **Year of fee payment:** 08
Dec 31, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** GB **Payment date:** 20080416 **Year of fee payment:** 08
Oct 31, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** CH **Payment date:** 20080702 **Ref country code:** IE **Payment date:** 20080415 **Ref country code:** NL **Payment date:** 20080403 **Year of fee payment:** 08 **Ref country code:** SE

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			Payment date: 20080408
Sep 30, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** BE **Payment date:** 20080616 **Ref country code:** FI **Payment date:** 20080411 **Year of fee payment:** 08 **Ref country code:** IT **Payment date:** 20080428
Aug 29, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** AT **Payment date:** 20080410 **Year of fee payment:** 08
Jul 31, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** DE **Payment date:** 20080417 **Ref country code:** DK **Payment date:** 20080430 **Ref country code:** ES **Payment date:** 20080520 **Year of fee payment:** 08 **Ref country code:** FR **Payment date:** 20080312
May 30, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** GR **Payment date:** 20070402 **Year of fee payment:** 07 **Ref country code:** PT **Payment date:** 20080328 **Year of fee payment:** 08
Apr 30, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** FR **Payment date:** 20070411 **Year of fee payment:** 07
Jan 2, 2008	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** IT **Payment date:** 20070515 **Year of fee payment:** 07
Nov 24, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** CH **Payment date:** 20070702 **Year of fee payment:** 07 **Ref country code:** GB **Payment date:** 20070411
Jun 15, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** BE **Payment date:** 20070615 **Year of fee payment:** 07
May 21, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** ES **Payment date:** 20070521 **Year of fee payment:** 07
Apr 16, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** DK **Payment date:** 20070416 **Year of fee payment:** 07
Apr 13, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** FI **Payment date:** 20070413 **Year of fee payment:** 07
Apr 12, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** AT **Payment date:** 20070412 **Year of fee payment:** 07 **Ref country code:** IE
Apr 5, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** DE **Payment date:** 20070405 **Year of fee payment:** 07
Apr 4, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** SE **Payment date:** 20070404 **Year of fee payment:** 07

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Apr 3, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** NL **Payment date:** 20070403 **Year of fee payment:** 07
Mar 28, 2007	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** PT **Payment date:** 20070328 **Year of fee payment:** 07
Jun 28, 2006	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** CH **Payment date:** 20060628 **Year of fee payment:** 06
Apr 30, 2006	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** IT **Payment date:** 20060430 **Year of fee payment:** 06
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Apr 10, 2006	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** FR **Payment date:** 20060410 **Year of fee payment:** 06
Mar 29, 2006	PGFP	Postgrant: annual fees paid to national office	**Ref country code:** GR **Payment date:** 20060329 **Year of fee payment:** 06
Oct 27, 2004	26N	No opposition filed	**Effective date:** 20040806
Jul 30, 2004	ET	Fr: translation filed	
Jul 1, 2004	REG	Reference to a national code	**Ref country code:** ES **Ref legal event code:** FG2A **Ref document number:** 2210056 **Kind code of ref document:** T3
Apr 30, 2004	PG25	Lapsed in a contracting state announced via postgrant inform. from nat. office to epo	**Ref country code:** MC **Free format text:** LAPSE BECAUSE OF NON-PAYMENT OF DUE FEES **Effective date:** 20040430
Apr 12, 2004	PG25	Lapsed in a contracting state announced via postgrant inform. from nat. office to epo	**Ref country code:** LU **Free format text:** LAPSE BECAUSE OF NON-PAYMENT OF DUE FEES **Effective date:** 20040412
Mar 31, 2004	REG	Reference to a national code	**Ref country code:** PT **Ref legal event code:** SC4A **Free format text:** AVAILABILITY OF NATIONAL TRANSLATION **Effective date:** 20040204
Mar 15, 2004	REG	Reference to a national code	**Ref country code:** DK **Ref legal event code:** T3
Feb 10, 2004	REG	Reference to a national code	**Ref country code:** SE **Ref legal event code:** TRGR
Feb 4, 2004	GBT	Gb: translation of ep patent filed (gb section 77(6)(a)/1977)	**Effective date:** 20040108
Dec 31, 2003	REG	Reference to a national code	**Ref country code:** IE **Ref legal event code:** FG4D **Free format text:** GERMAN
Dec 11, 2003	REF	Corresponds to:	**Ref document number:** 50100901 **Country of ref document:** DE **Date of ref document:** 20031211 **Kind code of ref document:** P
Nov 28, 2003	REG	Reference to a national code	**Ref country code:** CH **Ref legal event code:** NV **Representative=s name:** HANS RUDOLF GACHNANG PATENTANWALT
Nov 14, 2003	REG	Reference to a national code	**Ref country code:** CH **Ref legal event code:** EP

Date	Code	Event	Description
Nov 5, 2003	REG	Reference to a national code	**Ref country code:** GB **Ref legal event code:** FG4D **Free format text:** NOT ENGLISH
Nov 5, 2003	AK	Designated contracting states:	**Kind code of ref document:** B1 **Designated state(s):** AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
Nov 5, 2003	PG25	Lapsed in a contracting state announced via postgrant inform. from nat. office to epo	**Ref country code:** CY **Free format text:** LAPSE BECAUSE OF FAILURE TO SUBMIT A TRANSLATION OF THE DESCRIPTION OR TO PAY THE FEE WITHIN THE PRESCRIBED TIME-LIMIT **Effective date:** 20031105 **Ref country code:** TR
Jul 9, 2003	AKX	Payment of designation fees	**Designated state(s):** AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
Oct 16, 2002	AX	Extension or validation of the european patent to	**Free format text:** AL;LT;LV;MK;RO;SI
Oct 16, 2002	AK	Designated contracting states:	**Kind code of ref document:** A1 **Designated state(s):** AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
Oct 16, 2002	17P	Request for examination filed	**Effective date:** 20020228

Exhibit 6

ORIGINAL RESEARCH

RELATIVE BIOAVAILABILITY COMPARISON OF DIFFERENT COENZYME Q_{10} FORMULATIONS WITH A NOVEL DELIVERY SYSTEM

Zheng-Xian Liu, PhD; Carl Artmann, PhD

Commercial coenzyme Q_{10} (CoQ_{10}, ubiquinone) formulations are often of poor intestinal absorption. The relative bioavailability of CoQ_{10} has been shown in National Institutes of Health–funded clinical trials to be increased by its delivery system. We investigated the bioavailability of a new CoQ_{10} formulation based on a new and patented technology, VESIsorb, with 3 other commercially available CoQ_{10} products, an oil-based formulation and 2 solubilizates. This new CoQ_{10} formulation (commercially branded CoQsource) is a lipid-based formulation that naturally self-assembles on contact with an aqueous phase into an association colloid delivery system (hereafter "colloidal-Q_{10}"). Twenty healthy male and female subjects participated in a double blind, comparative (parallel design), controlled, single-dose (120 mg) bioavailability study. Plasma concentration of CoQ_{10} was determined at baseline and at various intervals after administration over a 24-hour period. To compare bioavailability, maximum concentration (C_{max}) and area under curve from 0 to >10 hours ($AUC_{(0\text{-}10h)}$) were assessed. The kinetic profiles of all CoQ_{10} preparations revealed a 1-peak plasma concentration-time course. Highest C_{max} values were seen after colloidal-Q_{10} administration. Colloidal-Q_{10} not only had the highest plasma concentration levels after 1 hour, but it continued to increase before reaching C_{max} at about 4 hours. The plasma concentration of colloidal-Q_{10} remained well above the levels of the 3 other products throughout the 24-hour period. The relative bioavailability calculated using the $AUC_{(0\text{-}10h)}$ values was also the highest for colloidal-Q_{10}; the $AUC_{(0\text{-}10h)}$ values were 30.6, 6.1, 4.9 and 10.7 µg/ml*h for colloidal-Q_{10}, solubilizate 1, the oil-based formulation, and solubilizate 2, respectively. Differences in C_{max} and AUC between colloidal-Q_{10} and the 3 other formulations were statistically significant. In summary, the data presented suggests that colloidal-Q_{10} improves the enteral absorption and the bioavailability of CoQ_{10} in humans. (*Altern Ther Health Med*. 2009;15(2):#-#.)

Zheng-Xian Liu, PhD, is chief executive officer of GeroNutra, Hayward, California, and Carl Artmann, PhD, is chief executive officer of Phacos GmbH, Gauting, Germany.

Disclosure

The work was funded by Vesifact AG, Baar, Switzerland, and performed at Phacos GmbH, Schrimpfstr. 49/3, D-82131 Gauting, Germany. Zheng-Xian Liu, PhD, is chief executive officer of GeroNutra and served as a paid consultant to SourceOne Global Partners in the preparation of this manuscript but holds no other financial interest in the products or technologies studied or in either Vesifact or SourceOne. Carl Artmann, PhD, is chief executive officer of Phacos GmbH and served as paid consultants to Vesifact in monitoring and analyzing this study but holds no other financial interest in the products or technologies studied or in either Vesifact or SourceOne.

Coenzyme Q_{10} (CoQ_{10}) plays a key role in mitochondrial cell physiology and is a powerful systemic antioxidant. Its chemical structure is shown in Figure 1. In certain conditions, the body's capacity for adequate CoQ_{10} homeostasis is impaired. In such situations, supplementation with CoQ_{10} has been shown to be beneficial.

Due to its poor solubility in water and its relatively high molecular weight (M_r=863) the oral bioavailability of CoQ_{10}, when administered as a powder, is low.[1,2] In the past several years, extensive efforts have been made to improve the oral bioavailability of CoQ_{10}. Examples of formulation strategies aimed at improving the enteral absorption of CoQ_{10} include oil-based formulations, solubilized formulations, and molecular complexes.[3-10] Several of these strategies have been shown to improve the bioavailability of CoQ_{10} as evidenced by their enhanced plasma CoQ_{10} response.

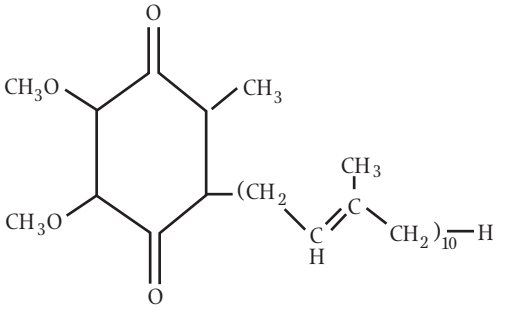

FIGURE 1 Chemical Structure of Coenzyme Q10

It is known that poorly water-soluble supplements (eg, fat-soluble vitamins) are better absorbed when administered after a meal containing fat. One of the reasons for the improved absorption is the enhanced drug solubilization by bile salt-mixed micelles formed from the digestion products of dietary triglycerides (monoglyceride and fatty acids) and bile, a tool developed by nature. The task of naturally formed bile salt-mixed micelles, having a size <10 nm, is to transport the lipophilic molecules through the aqueous environment of the gastrointestinal (GI) tract and across the unstirred water layer to the absorptive epithelium. VESIsorb, a new delivery technology, mimics this natural absorption process to improve bioavailability of poorly water-soluble drugs. The data presented suggest that colloidal-Q_{10}, a CoQ_{10} formulation based on this delivery system, improves the enteral absorption and the bioavailability of CoQ_{10} in humans.

MATERIALS AND METHODS

Design

A double-blind, comparative, controlled (parallel design), single-dose pharmacokinetic study with random assignment of subjects of both sexes was planned. The protocol was approved by the Grosshadern Hospital of Munich ethics commission, and informed consent was obtained from all subjects.

Subjects

Four groups (n=5, n=5, n=5, n=5) of clinically healthy men and women between the ages 18 and 60 years were recruited. Subjects were selected in accordance with the inclusion and exclusion criteria from among the group at Grosshadern Hospital and its facilities. The subjects were informed at the beginning about the nature of the study, its aims, and its execution. The data were acquired and stored in anonymous form.

Inclusion Criteria

- Men and women aged 18 to 60 years
- Clinically healthy, normal body mass index (18.5-25)
- No abnormalities in internal medical history
- No abnormalities in laboratory status
- Subject's agreement to participation in the study

Exclusion Criteria

- Men and women aged under 18 or over 60 years
- Previous history of hematological diseases (eg, known susceptibility to thrombosis)
- Pathological laboratory status (blood count, thrombocytes)
- Medication with vasoactive substances
- Medication affecting coagulation (eg, acetyl salicylic acid, aspirin)
- Medication affecting cholesterol (eg, statins)
- Diabetes
- Skin diseases (acute, chronic, allergic)
- Malignant tumors
- Disorders of heart, kidney, lung, or liver function
- Feverous or infectious diseases
- Alcohol or drug abuse
- Pregnancy or lactation
- Participation in power sports activities or sport activities during the study
- Failure to submit a statement of consent
- Participation in another clinical study within 4 weeks preceding this study or during this study
- Probable noncompliance of the subject; insufficient reliability

Study Preparations

- Product A (colloidal-Q_{10}): 30 mg CoQ_{10} per capsule
- Product B (solubilizate 1): 60 mg CoQ_{10} per capsule
- Product C (oil-based formulation): 30 mg CoQ_{10} per capsule
- Product D (solubilizate 2): 30 mg CoQ_{10} per capsule

Product A was provided by Vesifact AG, Baar, Switzerland. Products B, C, and D are commercially available CoQ_{10} products.

Intervention

Subjects (12 females, 8 males) qualifying for the study on the basis of the inclusion and exclusion criteria were randomized to consume a single oral dose of 120 mg CoQ_{10} in the form of one of the following study preparations:

- 4 capsules of product A (colloidal-Q_{10})
- 2 capsules of product B (solubilizate 1)
- 4 capsules of product C (oil-based formulation)
- 4 capsules of product D (solubilizate 2)

The study preparations were given in the morning before breakfast, on an empty stomach. The taking of blood samples and mealtimes occurred at predetermined regular time intervals (Table 1). For a controlled diet, the same food was eaten among

TABLE 1 Blood Sampling and Mealtimes

Day	Time	Action	Time Elapsed (after CoQ10 intake)
1	07:30-08:00	Blood sample, zero value, empty stomach Administration of 120 mg CoQ10	
	08:00-08:30	Breakfast	
	08:30-09:00	Blood sample	1 h
	09:30-10:00	Blood sample	2 h
	10:30-11:00	Blood sample	3 h
	11:30-12:00	Blood sample	4 h
	12:00-12:30	Lunch	
	12:30-13:00	Blood sample	5 h
	13:30-14:00	Blood sample	6 h
	15:30-16:00	Blood sample	8 h
	17:30-18:00	Blood sample	10 h
	18:00-18:30	Dinner	
2	08:30-09:00	Blood sample, empty stomach	24 h

groups. No other food was eaten (control of compliance).

Analysis of Plasma Samples

Plasma concentration of CoQ_{10} were determined by high-performance liquid chromatography (HPLC) using a Merck/Hitachi HPLC system equipped with an auto sampler (Spectra Physics, Newport Corp, Mountain View, California), a UV detector and an analytical column (Nucleosil RP 18, 5µm, 150 mm x 4 mm, Merck, Whitehouse Station, New Jersey). CoQ_{10} was eluted with acetonitrile and detected at 275 nm.

Statistical Analysis

Data were analysed using GraphPad Prism 3.0 software (GraphPad Software Inc, San Diego, California). For descriptive purposes, the mean and standard deviations of the mean were calculated. The homogeneity of the CoQ_{10} baseline levels at the beginning of the study was statistically evaluated using analysis of variance (ANOVA) and Tukey's multiple comparison test (post hoc test). To assess pharmacokinetic parameters, the area under the observed concentration-time curve above baseline ($AUC_{0\text{-}10h}$) and the observed maximum plasma concentration above baseline (Delta C_{max}) were calculated individually for each volunteer. The AUC and Delta C_{max} were compared after log transformation using ANOVA with the post-hoc Dunnett's multiple comparison test.

A probability level of $P<.05$ was considered to indicate statistical significance.

RESULTS

The pharmacokinetic characteristics of the 4 CoQ_{10} study preparations after a single oral intake of 120 mg CoQ_{10} are summarized in Table 2 and Figure 2. The data show that the mean plasma CoQ_{10} values at baseline were similar in the 4 groups, ranging from 0.75 to 0.90 µg/mL. There was no statistically significant difference between groups A to D (P=.1402). There was a significant increase in CoQ_{10} plasma levels following supplementation in all 4 groups. The kinetic profiles of all 4 preparations revealed a 1-peak plasma concentration-time course. Maximum plasma level was reached between 3 and 5 hours after oral administration. The highest C_{max} values were seen after colloidal-Q_{10} application. Colloidal-Q_{10} had the highest plasma concentration level after 1 hour, and it continued to increase before reaching C_{max} at about 4 hours. The plasma concentration level of colloidal-Q_{10} remained well above the levels associated with the 3 other products throughout the 24-hour period. The relative bioavailability calculated using the $AUC_{(0\text{-}10h)}$ values was also the highest for colloidal-Q_{10}; the $AUC_{(0\text{-}10h)}$ values were 30.6, 6.1, 4.9 and 10.7 µg/ml*h for product A (colloidal-Q_{10}), product B (solubilizate 1), product C (oil-based formulation) and product D (solubilizate 2), respectively. Differences in Delta C_{max} and $AUC_{(0\text{-}10h)}$ between colloidal-Q_{10} and the 3 other formulations were statistically significant. Looking at the $AUC_{(0\text{-}10h)}$, the relative bioavailability of product A was 622% compared to C, 499% to product B, and 286% to product D.

DISCUSSION

The absorption of most drugs depends on 2 processes: (1) the dissolution of the drug in physiological fluids and (2) the absorption process itself (ie, the process by which a drug in solution enters the cells at the absorption site and finally enters general blood circulation). Many drugs are absorbed by passive diffusion (ie, a spontaneous migration of drug molecules from a region of high concentration to a region of low concentration). Other drugs are absorbed by facilitated or active transport, which involves the expenditure of energy by the body. In either event, the dissolution of the drug is the first step in the absorption process unless the drug is administered as a solution. On the

TABLE 2 Pharmacokinetic Parameters of the Four Study Preparations Determined After a Single Oral Intake of 120 mg CoQ_{10}

		Product A (Colloidal-Q10)	Product B (Solubilizate 1)	Product C (Oil-based formulation)	Product D (Solubilizate 2)
Baseline	[µg/mL]				
	Mean	0 90	0.76	0.82	0.75
	SD	0.12	0.11	0.10	0.09
Delta C_{max}	[µg/mL]				
	Mean	5 99	1.68	1.42	2.98
	SD	0.41	0.33	0.39	0.55
C_{max}	[µg/mL]				
	Mean	6.89	2.44	2.24	3.73
	SD	0.51	0.31	0.30	0.49
T_{max}	[h]				
	Mean	4.20	3.40	5.00	4.20
	SD	0.45	0.55	0.00	0.45
$AUC_{(0\text{-}10h)}$	[µg/mL*h]				
	Mean	30.62	6.14	4.92	10.71
	SD	4.24	0.16	1.96	2.35

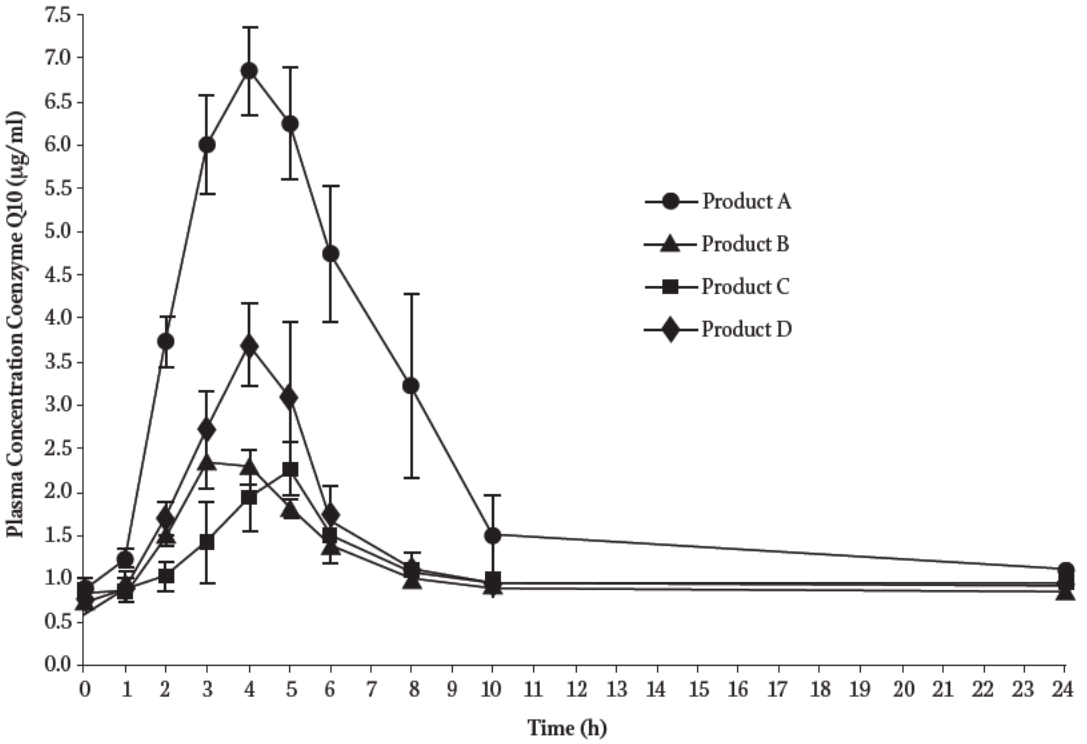

FIGURE 2 Changes in Plasma CoQ10 Concentrations After a Single Oral Intake of 120 mg CoQ10 (n = 20)*

*Product A: colloidal-Q_{10}; product B: solubilizate 1; product C: oil-based formulation; product D: solubilizate 2.

other hand, some drugs are absorbed by the process of pynocytosis or endocytosis, which involves the engulfing of solid particles and the incorporation of such particles into the cellular contents.

To compensate for the poor absorption displayed by many drugs, a formulation may use one or more mechanisms to increase the extent to which the administered drug is absorbed. There are vast numbers of such techniques, which can be grouped into the following broad categories: (1) enhancement of the rate and extent of dissolution and (2) facilitation of an absorption process. Formulating a drug with an oil for the purpose of involving the lymphatic system in the absorption of the drug is an example of the second technique. VESIsorb, the delivery system of colloidal-Q_{10} is an example of the first technique.

VESIsorb was designed to address the poor bioavailability of drugs and natural bioactives like CoQ_{10} exhibiting poor water solubility but high membrane permeability (Biopharmaceutical Classification System: Class II compounds). This delivery system is a lipid-based formulation that self-assembles on contact with an aqueous phase into a colloidal delivery system. The co-administered drug and/or natural bioactive will be solubilized by the in situ formed colloidal system with a mean diameter of <100 nm and a very narrow size distribution as assessed by dynamic laser light scattering using a Zetasizer Nano (Malvern, Worcestershire, United Kingdom). This colloidal solubilization improves the transport of the drug through the aqueous phase of the GI-lumen to the absorptive epithelium, hence its bioavailability. The improvement of oral drug or natural bioactive bioavailability by this technology is broken down into 3 steps: (1) formation of the colloidal delivery system, (2) diffusion across the unstirred water layer, and (3) transfer to the absorption epithelium.

Similar to vitamin E and other lipophilic substances, CoQ_{10} is absorbed, at least partially, by the lymphatic route.[1] Lymphatic absorption involves the following steps: (1) incorporation of CoQ_{10} into lipoproteins/chylomicrons within the enteroyte, (2) secretion of the lipoproteins/chylomicrons from the enterocyte into the lymph vessel, and (3) transport of the lipoproteins/chylomicrons within the lymph vessel to the blood stream. Adequate stimulation of the lipoprotein/chylomicron production is thus of paramount importance for optimal CoQ_{10} absorption by the lymphatic route. This can be achieved by administering CoQ_{10} with or after a meal containing some fat.

CoQ_{10} exhibits non-linear pharmacokinetics (ie, the fraction of a single dose absorbed falls as the dose increases).[11-13] For example, it has been shown that divided dosages (2 x 100 mg) of CoQ_{10} caused a larger increase in plasma levels of CoQ_{10} than a single dose of 200 mg.[12] Larger daily doses of CoQ_{10} should therefore be divided into several doses. Dividing the daily CoQ_{10} dose into several doses will not only maximize the CoQ_{10} absorption, but also reduce the difference between maximal and minimal steady states plasma levels of CoQ_{10}.

In the current study, the posttreatment CoQ_{10} plasma levels of all 4 products are relatively high in comparison to those reported previously. It is difficult to compare the results of this study to other studies: inter-study comparisons are difficult to

make, as variables from food intake to dosing strategy to plasma lipoprotein levels to analytic procedures may affect the results. And there is substantial variation in people's ability to absorb CoQ_{10} in the normal population.[5,14] Additional clinical studies are indicated to verify that the improved absorption with colloidal-Q_{10} correlates with clinical response to treatment.

In the course of the last 25 years of clinical research in treating heart failure of diverse etiology with supplemental CoQ_{10}, it became clear that the initial strategy of normalizing plasma CoQ_{10} status was not effective. Only patients with plasma CoQ_{10} levels >2.5 µg/mL showed significant clinical improvement in heart failure. In fact, therapeutic plasma CoQ_{10} levels are now considered to be > 3.5 µg/ml.[15] Likewise, the pilot trial of CoQ_{10} in patients with Parkinson's disease showed that the benefit was greatest in subjects receiving the highest dosage (1200 mg/d).[16] Thus, a CoQ_{10} formulation exhibiting good CoQ_{10} bioavailability is of great value.

The safety of CoQ_{10}, even at high dosages, is well documented. In particular, a 52-week study revealed no toxicity at a dose of 1200 mg/kg/day,[17] based on which the acceptable daily intake (ADI) for adults weighing 50 kg was estimated to be 600 mg/day. It was also reported in clinical studies of patients with early Parkinson's disease (up to 1200 mg/day for 16 months),[15] Huntington's disease (600mg/day for 30 months),[18] and heart diseases (50-150 mg/day for 3 months)[19] that the frequency of side effects was almost equal to that in the control groups, indicating that the dosage levels examined were within the limits of tolerable intake. In a recent study, the safety profile of CoQ_{10} at high doses for healthy subjects was assessed. CoQ_{10} in capsule form was taken for 4 weeks at doses of 300, 600, and 900 mg/day by a total of 88 adult volunteers. The findings of the study showed that CoQ_{10} was well-tolerated and safe for healthy adults at an intake of up to 900 mg/day.[20] Furthermore, each component of colloidal-CoQ_{10} is Generally Regarded as Safe (GRAS) per the FDA's Code of Federal Regulations (CFR 21) and European regulatory standards, which guarantees the wholesomeness and safety of each ingredient for human consumption. Essentially, it is the FDA's assurance that all ingredients used in food products have undergone toxicological and safety testing to guarantee their safe use in foods.

In summary, this study compared the relative bioavailability of colloidal-Q_{10} with that of 3 commercially available products, 2 CoQ_{10} solubilizates and an oil-based CoQ_{10} formulation after a single oral administration of 120 mg. Our data suggest that the enteral absorption and bioavailability of CoQ_{10} can be enhanced by colloidal-Q_{10} that mimics the naturally occurring mixed micellar transport system of the human body. This also increases the likelihood that this technology can be considered as safe for improving the absorption of drugs with low water solubility. Current research is investigating whether this technology also can be used to improve the absorption of other natural lipophilic actives, such as omega-3, vitamin D, resveratrol, tocotrienols, flavonoids, and gamma-tocopherols.

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Exhibit 7

Why is Qunol the better CoQ10?

Patented Water and Fat Soluble CoQ10

	Qunol ULTRA CoQ10	Regular CoQ10*
Process	100% natural CoQ10	may contain synthetic CoQ10
Source	made through fermentation	may be made from tobacco leaves
Absorption	great absorption (300% better)	poor absorption
USP Test	dissolution test: PASS	dissolution test: FAIL
CoQ10 Solubility	100% water soluble	does not dissolve in water
Fat Solubility	100% fat soluble	dissolves poorly in oils and fat

With Qunol ULTRA CoQ10, optimum blood levels of CoQ10 are reached in just weeks – not months, as with regular CoQ10.

*Regular CoQ10 refers to unsolubilized Ubiquinone in oil suspensions in softgels and/or powder-filled capsules/tablets.

ACTUAL PILL SIZE

Directions: Adults: Take one (1) softgel, once per day with food, or as recommended by your healthcare professional.

Supplement Facts

Serving Size: 1 Softgel
Servings per Container: 30

	Amount Per Softgel	% Daily Value
Vitamin E (as dl-alpha tocopheryl acetate)	150 IU	500%
Coenzyme Q10 (Ubiquinone USP Grade)	100mg	*

*Daily Value not established

Other Ingredients: gelatin, polysorbate 80, medium-chain triglycerides, glycerin, hydroxylated lecithin, sorbitol, purified water, annatto suspension in sunflower oil. **Contains Soy.**

Free of: milk and milk by-products, egg and egg by-products, fish, shellfish, tree nuts, peanuts/peanut oil, wheat, gluten, starch, yeast.

This product is a GLUTEN FREE product.

WARNING: KEEP OUT OF REACH OF CHILDREN. If you are pregnant or nursing a baby, seek the advice of a health professional before using this product.

THE BOTTLE CAP ON THIS PRODUCT IS SECURED WITH AN IMPRINTED PLASTIC SEAL. DO NOT USE THIS PRODUCT IF SEAL IS CUT, TORN, BROKEN OR MISSING.

Keep bottle tightly closed. Store between 15°-30°C (59°-86°F). Do not refrigerate.

Manufactured for and distributed by Quten Research Institute, LLC
39 Plymouth Street, Fairfield, NJ 07004
1-877-290-2621 **www.qunol.com**

MONEY BACK GUARANTEE

Manufactured under one or more of the following U.S. patents: 6,056,971, 6,300,377 and 6,740,338. MADE IN THE USA

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Qunol™ ULTRA CoQ10

Patented Water and Fat Soluble CoQ10

Qunol™ ULTRA CoQ10

100% NATURAL CoQ10

100 mg | Pharmaceutical Grade Clinical Strength

100 mg = 100 mg 100 mg 100 mg

ULTRA CoQ10 — 300mg Regular CoQ10

3X BETTER ABSORPTION

1 Month Supply

Dietary Supplement — **100 mg 30 softgels**

Qunol™

The Gold Standard in CoQ10

- **SUPPORTS** heart and vascular health
- **PROMOTES** healthy blood pressure levels
- **ESSENTIAL** for energy production
- **BENEFICIAL** to Statin drug users
- **POWERFUL** all-natural antioxidant

† Helps maintain healthy blood pressure already within a normal range.

† Cholesterol-lowering Statin drugs can deplete the body's natural levels of CoQ10. Qunol can help replenish lost CoQ10 due to Statin drug therapy.

Exhibit 8

eurofins | Supplement Analysis Center

Eurofins Scientific Inc.
Supplement Analysis Center
1365 Redwood Way
Petaluma, CA 94954
Tel.+1 707 792 7300
Fax:+1 707 792 7309

July 21, 2014

Jack Fitzgerald
The Law Office of Jack Fitzgerald, PC
2870 4th Avenue
Suite 205
San Diego, CA 92103

CERTIFICATE OF ANALYSIS

AR-14-KK-011885-01

Batch #: EUCAPE-00056352

Sample Identification:

Sample #: 740-2014-00011317
Description: Coenzyme Q-10 100mg Softgel Supplement #1, Lot #G13NM13, Exp. 03/15
Condition: Softgels in a white plastic bottle received at room temperature.
Date Received: July 07, 2014

KK106: Dissolution of Nutritional Supplements by USP/NF
Method Reference: USP

Completed: 07/21/2014	**Result**	**Theoretical Level**
Dissolution	Done	

KK130: Average content weight
Method Reference: Not applicable

Completed: 07/21/2014	**Result**	**Theoretical Level**
Average content weight	540.70 mg/softgel	

KK167: Client Supplied Method (HPLC)
Method Reference: Internal Method

Completed: 07/21/2014	**Result**	**Theoretical Level**
Ubidecarenone (Strength Test)	96.3 mg/softgel	
Ubidecarenone (Dissolution)(Water)	<2 mg/softgel	
Ubidecarenone (Dissolution)(Pepsin)(retest)	45.3 mg/softgel	

KK169: Client Supplied Method (WT/UV)
Method Reference: Not applicable

Completed: 07/21/2014	**Result**	**Theoretical Level**
Ubidecarenone (Disintegration)(Water)	>60 minute	
Ubidecarenone (Disintegration)(Pepsin)(retest)	47 minute	

eurofins

Sample #: 740-2014-00011317

The Law Office of Jack Fitzgerald, PC
2870 4th Avenue
Suite 205
San Diego, CA 92103

Results pertain only to the items tested.
Estimation of uncertainty of measurement is available upon request.

Mariel Esguerra
Technical Accounts Manager

eurofins | Supplement Analysis Center

Eurofins Scientific Inc.
Supplement Analysis Center
1365 Redwood Way
Petaluma, CA 94954
Tel.+1 707 792 7300
Fax:+1 707 792 7309

July 21, 2014

Jack Fitzgerald
The Law Office of Jack Fitzgerald, PC
2870 4th Avenue
Suite 205
San Diego, CA 92103

CERTIFICATE OF ANALYSIS

AR-14-KK-011891-01

Batch #: EUCAPE-00056352

Sample Identification:

Sample #: 740-2014-00011318
Description: Coenzyme Q-10 100mg Softgel Supplement #2, Lot #1341-2121, Exp. 03/2016
Condition: Softgels in a white plastic bottle received at room temperature.
Date Received: July 07, 2014

KK106: Dissolution of Nutritional Supplements by USP/NF
Method Reference: USP
Completed: 07/21/2014

	Result	Theoretical Level
Dissolution	Done	

KK130: Average content weight
Method Reference: Not applicable
Completed: 07/21/2014

	Result	Theoretical Level
Average content weight	943.85 mg/softgel	

KK167: Client Supplied Method (HPLC)
Method Reference: Internal Method
Completed: 07/21/2014

	Result	Theoretical Level
Ubidecarenone (Strength Test)	95.4 mg/softgel	
Ubidecarenone (Dissolution)(water)	92.7 mg/softgel	

KK169: Client Supplied Method (WT/UV)
Method Reference: Not applicable
Completed: 07/21/2014

	Result	Theoretical Level
Ubidecarenone (Disintegration)(water)	13 minute	

Results pertain only to the items tested.
Estimation of uncertainty of measurement is available upon request.

Mariel Esguerra
Technical Accounts Manager

Exhibit 9

ABC Testing

Advanced Botanical Consulting & Testing, Inc.
1169 Warner Ave., Tustin, CA 92780, Phone: (714) 259-0384 Fax: (714) 259-0385

Lang Pharma Nutrition Inc.
20 Silva Lane
Middletown, RI 02842
Tel.: (401) 848-7700/ (401) 848-6211 (E. Kahn, Direct)
Fax: (401) 848-7701

ATTN: Ellen Kahn
P. O. #:

Client Sample ID: CVS Ultra CoQ-10 (60 softgels)
Lot #: F12NM10 (Stability 18M@ 40C/75%RH)

Lab #: 87002

Received Date: 08/08/2012
Date In: 08/08/2012
Date Out: 02/06/2014
Report Date: 02/18/2014

Analyses	Results
Color (Visual)	Orange/red softgels
Odor (Organoleptic)	Citrus/fruity
Coenzyme Q10 (HPLC)	101.72 mg/softgel
Moisture content (Karl Fischer)	2.16 % (content only)
Rupture (USP)	Fail, >30 min
Average fill weight (based on 10)	533.03 mg/softgel

Method: ASTA method manual, ALC151A, USP36/NF31

Analyzed by: _____ Chemist

Approved by: _____ Wendi Wang, PhD, President

Exhibit 10

Tampa Bay Analytical Research, Inc.
13130 56th Court STE 606 Clearwater, FL 33760 USA
Ph: 727-540-0900 Fax: 727-540-0922

Assay Result Form

Number:	ARF-TM05446	Sample Name:	CoQ10		
Control Number:	TM05446	Sample Lot #:	#1		
Customer Name:	Law Offices of J.F.	Address:	San Diego, CA		
Date:	11/22/2013	Project #:	PR2124	Version:	2

Analyte	Method Reference	Specification	Result	Date Tested	Notebook Reference
CoQ10 Capsule 1	TBAR-TM-012 Dissolution	NA	**None Detected** Notes :a,b	11/18/2013	TBAR-110-95
CoQ10 Capsule 2		NA	**None Detected** Notes: b		
CoQ10 Capsule 3		NA	**27.9 mg** Notes: c		
CoQ10 Capsule 4		NA	**0.578 mg** Notes: b		
CoQ10 Capsule 5		NA	**None Detected** Notes: b		
CoQ10 Capsule 6		NA	**None Detected** Notes : b		

Notes:

a. Ubidecarenone reference standard: Kaneka lot S376, 99.9% purity

b. No visible rupture observed after 60 minutes

c. Approximate rupture time of 50 minutes

Documentation to support these results is on file at Tampa Bay Analytical Research. All quantitative results are rounded to three (3) significant figures. This product analysis is for the benefit of the client only, and results are applicable only to the test material submitted to Tampa Bay Analytical Research, and can not be applied to any other test material or sample. It is the responsibility of the client to determine the suitability of the information provided in this report for their specific use.

File: \\TBAR-2\Documents (E:)\QualityManual\SOPs\Forms\5.8.01-F2

Written By: Robert Arce
Robert Arce
Quality Assurance Manager
Digitally signed by Robert Arce
DN: cn=Robert Arce c=US o=Tampa Bay Analytical Research, Inc. ou=Tampa Bay Analytical Research, Inc. e=rarce@tampabayanalytical.com
Reason: I am the author of this document
Location:
Date: 2013-11-22 09:26-05:00

Approved By:
Mark Roman
President
Digitally signed by Mark C. Roman
DN: cn=Mark C. Roman gn=Mark C. Roman c=United States l=US o=Tampa Bay Analytical Research, Inc. e=mroman@tampabayanalytical.com
Reason: I am approving this document
Location: Clearwater, FL
Date: 2013-11-22 09:40-05:00

Tampa Bay Analytical Research, Inc.
13130 56th Court STE 606 Clearwater, FL 33760 USA
Ph: 727-540-0900 Fax: 727-540-0922

Assay Result Form

Number:	ARF-TM05447	Sample Name:	CoQ10		
Control Number:	TM05447	Sample Lot #:	#2		
Customer Name:	Law Offices of J.F.	Address:	San Diego, CA		
Date:	11/22/2013	Project #:	PR2124	Version:	2

Analyte	Method Reference	Specification	Result	Date Tested	Notebook Reference
CoQ10 Capsule 1	TBAR-TM-012 Dissolution	NA	**None Detected** Notes :a, b	11/18/2013	TBAR-110-95
CoQ10 Capsule 2		NA	**None Detected** Notes: b		
CoQ10 Capsule 3		NA	**27.6 mg** Notes: c		
CoQ10 Capsule 4		NA	**0.720 mg** Notes: b		
CoQ10 Capsule 5		NA	**0.564 mg** Notes: b		
CoQ10 Capsule 6		NA	**None Detected** Notes: b		

Notes:

a. Ubidecarenone reference standard: Kaneka lot S376, 99.9% purity

b. No visible rupture observed after 60 minutes

c. Approximate rupture time of 50 minutes

Documentation to support these results is on file at Tampa Bay Analytical Research. All quantitative results are rounded to three (3) significant figures. This product analysis is for the benefit of the client only, and results are applicable only to the test material submitted to Tampa Bay Analytical Research, and can not be applied to any other test material or sample. It is the responsibility of the client to determine the suitability of the information provided in this report for their specific use.

File: \\TBAR-2\Documents (E:)\QualityManual\SOPs\Forms\5.8.01-F2

Written By: Robert Arce
Robert Arce
Quality Assurance Manager
Digitally signed by Robert Arce
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Reason: I am the author of this document
Location:
Date: 2013-11-22 10:04-05:00

Approved By:
Mark Roman
President
Digitally signed by Mark C. Roman
DN: cn=Mark C. Roman gn=Mark C. Roman c=United States l=US o=Tampa Bay Analytical Research, Inc. e=mroman@tampabayanalytical.com
Reason: I am approving this document
Location: Clearwater, FL
Date: 2013-11-22 10:39-05:00

Exhibit 11

ABC Testing

Advanced Botanical Consulting & Testing, Inc.
1169 Warner Ave., Tustin, CA 92780, Phone: (714) 259-0384 Fax: (714) 259-0385

Lang Pharma Nutrition Inc.
20 Silva Lane
Middletown, RI 02842
Tel.: (401) 848-7700/ (401) 848-6211 (E. Kahn, Direct)
Fax: (401) 848-7701

ATTN: Ellen Kahn
P. O. #: 20130905

Client Sample ID: CoQ10 w/ VesiSorb (30 softgels)
Item#: C13NM29
Lot #:1211031, Exp. 01/15
Lab #: 104609

Received Date: 09/06/2013

Report Date: 09/10/2013

Analyses	Results	%Dissolved
CoQ10 (HPLC)	93.44 mg/ softgel	
Dissolution (500ml H2O, 75RPM, 37.5C)		
CoQ10 (HPLC)--when directly filtered & injected	36. 23mg/softgel*	39%
CoQ10 (HPLC)-when using IPA in 5:1 ratio to dilute out the aqueous dissolution medium	110.22 mg/softgel	118%
Average fill weight (based on 10)	539.25 mg/ softgel	

Method: ALC151A, USP36/NF31

* CoQ10 in the softgels once ruptured was physically suspended in the dissolution medium, not chemically solublized. If the solution is directly filtered and injected, the unsolublized portion is removed by the filtration step, which lead to low result. The dissolution sample needs to be properly diluted with organic solvent like isopropyl alcohol to assure complete solublization of the CoQ10, prior to injection into the HPLC. The above 2 results are firm confirmation of the concept. Results are based on one pooled dissolution sample from 6 vessels. Result is based on one trial only

Analyzed by: _____ Chemist

Approved by: _____ Wendi Wang, PhD, President

Exhibit 12

COVANCE

Report Number: 852626-0
Report Date: 12-Aug-2013
Report Status: Final
Supercedes : 850236-0

Certificate of Analysis

[redacted]

Sample Name:	[redacted]	**Covance Sample:**	2304502
Project ID	[redacted]-20130802-0001	**Receipt Date**	02-Aug-2013
PO Number	Charge/VISA	**Receipt Condition**	Ambient temperature
Lot Number	Lot 1	**Login Date**	02-Aug-2013
Sample Serving Size	1 Softgel	**Storage Condition**	5 (+/- 3) degrees Celsius
		Number Composited	20
		Online Order	20

Analysis	Result
Calculated Sample Weight	
Entity Weight	0.7441 g
Coenzyme Q10 Dissolution	
Coenzyme Q10	48.2 mg/g
Coenzyme Q10	56.3 mg/g
Coenzyme Q10	54.5 mg/g
Coenzyme Q10	59.2 mg/g
Coenzyme Q10	57.5 mg/g
Coenzyme Q10	56.2 mg/g
Coenzyme Q10	35.9 mg/Serving Size
% of Claim (100 mg/softgel)	35.9 %
Coenzyme Q10	41.9 mg/Serving Size
% of Claim (100 mg/softgel)	41.9 %
Coenzyme Q10	40.6 mg/Serving Size
% of Claim (100 mg/softgel)	40.6 %
Coenzyme Q10	44.1 mg/Serving Size
% of Claim (100 mg/softgel)	44.1 %
Coenzyme Q10	42.8 mg/Serving Size
% of Claim (100 mg/softgel)	42.8 %
Coenzyme Q10	41.8 mg/Serving Size
% of Claim (100 mg/softgel)	41.8 %
Dissolution	
Disintegrated in Specified Time Frame	yes

Method References	Testing Location
Calculated Sample Weight (PREP:8)	**Covance Laboratories - Madison**
Coenzyme Q10 Dissolution (Q10_S:4)	**Covance Laboratories - Madison**

Official Methods of Analysis of AOAC INTERNATIONAL, (2005) 18th ED., AOAC INTERNATIONAL Gaithersburg, MD, USA, Official Method 2008.07.

COVANCE

Report Number:	**852626-0**
Report Date:	**12-Aug-2013**
Report Status:	**Final**
Supercedes :	**850236-0**

Certificate of Analysis

[redacted]

Method References	Testing Location
Dissolution (DISL:4)	**Covance Laboratories - Madison**

United States Pharmacopeia, Thirty Fourth Revision, <2040>, <711>, United States Pharmacopeial Convention, Inc.: Rockville, Maryland (2011).

Client Supplied Method

Testing Location(s)	Released on Behalf of Covance by
Covance Laboratories - Madison	**Lori Ross - Associate Director**

3301 Kinsman Blvd
Madison WI 53704
608-242-2712 x4170

These results apply only to the items tested. This certificate of analysis shall not be reproduced, except in its entirety, without the written approval of Covance.

COVANCE

Report Number:	852627-0
Report Date:	12-Aug-2013
Report Status:	Final
Supercedes :	850237-0

Certificate of Analysis

[redacted]

Sample Name:	[redacted]	**Covance Sample:**	2304503
Project ID	[redacted]-20130802-0001	**Receipt Date**	02-Aug-2013
PO Number	Charge/VISA	**Receipt Condition**	Ambient temperature
Lot Number	Lot 2	**Login Date**	02-Aug-2013
Sample Serving Size	1 Softgel	**Storage Condition**	5 (+/- 3) degrees Celsius
		Number Composited	20
		Online Order	20

Analysis	Result
Calculated Sample Weight	
Entity Weight	0.7435 g
Coenzyme Q10 Dissolution	
Coenzyme Q10	65.5 mg/g
Coenzyme Q10	55.7 mg/g
Coenzyme Q10	56.2 mg/g
Coenzyme Q10	53.9 mg/g
Coenzyme Q10	49.5 mg/g
Coenzyme Q10	52.4 mg/g
Coenzyme Q10	48.7 mg/Serving Size
% of Claim (100 mg/softgel)	48.7 %
Coenzyme Q10	41.4 mg/Serving Size
% of Claim (100 mg/softgel)	41.4 %
Coenzyme Q10	41.8 mg/Serving Size
% of Claim (100 mg/softgel)	41.8 %
Coenzyme Q10	40.1 mg/Serving Size
% of Claim (100 mg/softgel)	40.1 %
Coenzyme Q10	36.8 mg/Serving Size
% of Claim (100 mg/softgel)	36.8 %
Coenzyme Q10	39.0 mg/Serving Size
% of Claim (100 mg/softgel)	39.0 %
Dissolution	
Disintegrated in Specified Time Frame	Yes

Method References	Testing Location
Calculated Sample Weight (PREP:8)	**Covance Laboratories - Madison**
Coenzyme Q10 Dissolution (Q10_S:4)	**Covance Laboratories - Madison**

Official Methods of Analysis of AOAC INTERNATIONAL, (2005) 18th ED., AOAC INTERNATIONAL Gaithersburg, MD, USA, Official Method 2008.07.

COVANCE

Report Number:	852627-0
Report Date:	12-Aug-2013
Report Status:	Final
Supercedes :	850237-0

Certificate of Analysis

[redacted]

Method References	Testing Location
Dissolution (DISL:4)	**Covance Laboratories - Madison**

United States Pharmacopeia, Thirty Fourth Revision, <2040>, <711>, United States Pharmacopeial Convention, Inc.: Rockville, Maryland (2011).

Client Supplied Method

Testing Location(s)	Released on Behalf of Covance by
Covance Laboratories - Madison	**Lori Ross - Associate Director**

3301 Kinsman Blvd
Madison WI 53704
608-242-2712 x4170

These results apply only to the items tested. This certificate of analysis shall not be reproduced, except in its entirety, without the written approval of Covance.

Exhibit 13

THE LAW OFFICE
OF JACK FITZGERALD, PC
2850 4th Avenue, Suite 11 | San Diego, California 92103

August 23, 2013

VIA CERTIFIED MAIL, RETURN RECEIPT REQUESTED

Michael Terry Duke
President and Chief Executive Officer
Wal-Mart Stores, Inc.
702 Southwest Eighth Street
Bentonville, Arkansas 72716-0215

CT Corporation System
As Agent of Service for Wal-Mart Stores, Inc.
818 W. Seventh Street
Los Angeles, California 90017

Re: Notice of Violation of California Consumers Legal Remedies Act and Demand to Remedy; Notice of Breach of Warranties; and Notice of Duty to Preserve Evidence

Dear Mr. Duke & Whomever Else It May Concern:

This firm represents consumer Thamar Santisteban Cortina, who purchased Wal-Mart's Equate brand "High Absorption Co Q-10" dietary supplements for her own, household use. On behalf of Ms. Santisteban Cortina, a class of consumers who purchased Equate CoQ10, and the general public, I write to notify Wal-Mart of its violations of the California Consumers Legal Remedies Act, Cal. Civ. Code §§ 1750 *et seq.*, and its breaches of express and implied warranties, in connection with its sale of Equate CoQ10. Finally, I write to notify Wal-Mart of its duty to preserve relevant evidence.

Investigation of Wal-Mart's Equate CoQ10 Dietary Supplement

Equate CoQ10's label claims the product provides "Clinical Strength," "High Absorption," and "3 times better absorption." More generally, Equate's label claims to "support Heart Health," "Support[] heart and vascular health," "Promote[] health blood pressure levels," provide "Powerful natural antioxidants," and be "Essential for energy production," and "Beneficial to Statin Users." Finally, Equate's label claims consumers can "Compare to Qunol™ Ultra CoQ-10." These claims are, however, false and misleading.

The U.S. Pharmacopeial Convention, or USP, is a nonprofit scientific organization whose participants set standards for dietary supplements that are enforceable by the Food and Drug Administration. The USP monographs applicable to Coenzyme Q10 require, for effectiveness,

soft gel products like Equate to exhibit 75% dissolution. Ubidecarenone Capsules, USP 35 at 1462.

Independent laboratory analyses of two separate lots of Equate, demonstrate, however, that the product exhibits much lower dissolution than required, of approximately 40%. Because this means Equate fails to adequately dissolve in the stomach so as to provide consumers the product's full intended benefit, its claim to provide "clinical strength," "high absorption," and "3 times better absorption" than competing products, its more general claims to support heart health and benefit statin users, and its comparisons to competing products, are false and misleading. I have attached these reports for your review.

Notice of Violation of Cal. Civ. Code §§ 1750 *et seq.*

Pursuant to Cal. Civ. Code § 1782(a), Ms. Santisteban Cortina hereby notifies you that Wal-Mart's labeling of Equate violates the following provisions of section 1770 of the California's Consumers Legal Remedies Act:

- Misrepresenting the source, sponsorship, approval, or certification of goods or services (Cal. Civ. Code § 1770(a)(2));
- Misrepresenting the affiliation, connection, or association with, or certification by, another (*id.* § 1770(a)(3));
- Representing that goods or services have sponsorship, approval, characteristics, ingredients, uses, benefits, or quantities which they do not have or that a person has a sponsorship, approval, status, affiliation, or connection which he or she does not have (*id.* § 1770(a)(5));
- Representing that goods are original or new if they have deteriorated unreasonably or are altered, reconditioned, reclaimed, used, or secondhand (*id.* § 1770(a)(6));
- Representing that goods or services are of a particular standard, quality, or grade, or that goods are of a particular style or model, if they are of another (*id.* § 1770(a)(7));
- Disparaging the goods, services, or business of another by false or misleading representation of fact (*id.* § 1770(a)(8));
- Advertising goods or services with intent not to sell them as advertised (*id.* § 1770(a)(9)); and
- Representing that the subject of a transaction has been supplied in accordance with a previous representation when it has not (*id.* § 1770(a)(16)).

Ms. Santisteban Cortina, on behalf of herself, other purchases of Equate, and the general public, hereby demands that Wal-Mart correct, repair, replace, or otherwise rectify the Equate

CoQ10 in violation of § 1770. Specifically, Ms. Cortina demands that Wal-Mart (1) agree to provide class members who purchased Equate and make a claim full refunds; and (2) either (a) discontinue selling Equate CoQ10 so long as it does not demonstrate at least 75% dissolution, or (b) remove from Equate CoQ10's packaging the offending labeling claims, disclose that Equate CoQ10 does not meet the USP standard dissolution level, and engage in a corrective advertising campaign to alert previous purchasers that Equate's "clinical strength," "high absorption," and "3 times better absorption" claims were false and misleading.

If Wal-Mart does not, within 30 days after receiving this letter, initiate these corrective actions, Ms. Santisteban Cortina may, on behalf of herself and others, bring claims against Wal-Mart under the California Consumers Legal Remedies Act for actual and punitive damages.

Notice of Breach of Warranty

By this letter, Ms. Santisteban Cortina further notifies Wal-Mart that it has breached express and implied warranties in selling Equate CoQ10 to her and other consumers, based on the manufacturing defects discussed above. Wal-Mart expressly affirmed and promised that Equate CoQ10 provides three times more absorption than competing products, and this formed part of the basis of the bargain for these purchases. As described earlier, Equate CoQ10 does not adequately dissolve, and thus Wal-Mart has breached this and other express warranties, e.g., that Equate CoQ10 provides "clinical strength," "high absorption," generally supports heart health, is beneficial to statin users, and is comparable to competing products.

In addition to breaching its express warranties, Wal-Mart breached the implied warranties of merchantability and fitness because, as detailed above, Equate does not have the qualities Ms. Santisteban Cortina and other purchasers reasonably expect, and is not fit for its particular purpose of supplementing the body's natural CoQ10 production sufficiently to support heart health and benefit statin users.

To rectify these warranty breaches, Wal-Mart must refund Equate purchasers the amounts spent on the product.[1]

Notice of Duty to Preserve Evidence

"The obligation to preserve evidence arises when the party has notice that the evidence is relevant to litigation or when a party should have known that the evidence may be relevant to future litigation." *Fujitsu Ltd. v. Fed. Express Corp.*, 247 F.3d 423, 436 (2d Cir. 2001) (citation omitted); *see also Net-Com Servs. v. Eupen Cable USA, Inc.*, 2013 U.S. Dist. LEXIS 109810, at *6-7 (C.D. Cal. Aug. 5, 2013). Ms. Santisteban Cortina accordingly notifies Wal-Mart of its duty to preserve evidence relevant to the potential litigation that she may initiate if Wal-Mart does not

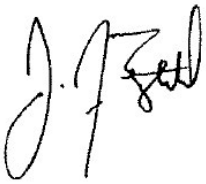
[1] Equate's packaging in fact *promises* "Satisfaction guaranteed – Or we'll replace it or give you your money back." Ms. Santisteban Cortina hereby invokes this provision on behalf of the putative class of Equate purchasers.

undertake the steps demanded herein. Wal-Mart should preserve all relevant documents, including without limitation, communications and other documents concerning Equate's manufacture, labeling, packaging, advertising, distribution, and sales, as well as samples of Equate lots currently in Wal-Mart's possession, custody, or control.

* * *

Although Ms. Santisteban Cortina will permit Wal-Mart a reasonable time to review this letter, and to reach out if it believes an early resolution may be possible, absent some indication that Wal-Mart intends to remedy the wrongs described herein, Ms. Santisteban Cortina intends to file shortly a class action in the United States District Court.

Very truly yours,



Jack Fitzgerald

Attachments

Jack Fitzgerald | jack@jackfitzgeraldlaw.com
Phone: (619) 692-3840 | Fax: (619) 362-9555

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Fax: (619) 564-6665

Counsel for Plaintiff and the Proposed Class

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

THAMAR SANTISTEBAN CORTINA, on behalf of herself, all others similarly situated and the general public,

Plaintiff,

v.

WAL-MART STORES, INC., and LANG PHARMA NUTRITION, INC.,

Defendants.

Case No: 3:13-cv-02054-BAS-DHB

CERTIFICATE OF SERVICE

I hereby certify that on April 23, 2015, I served the foregoing Second Amended Complaint on counsel for all parties by notice of electronic filing, which was automatically generated by the CM/ECF system at the time the document was filed with the Court.

Dated: April 23, 2015

/s/ Jack Fitzgerald
Jack Fitzgerald