K2VITAL® DELTA

MARKET STUDY: K2 STABILITY 2017

kappa BIOSCIENCE

K2VITAL® DELTA

K2VITAL® DELTA VITAMIN K2 STABILITY/ LABEL CLAIM MARKET STUDY – 2017 RESULTS

Vitamin K2 MK-7 is growing rapidly in global nutraceutical markets, mirroring market trends for vitamin D3. *Vitamin K2 regulates calcium transport in the body – it's critical for the maintenance of healthy bones and proper cardiovascular health. K2 integrates calcium into bone and prevents calcium build-up in arteries. Vitamin K2 is the key to vitality, supporting lifelong health by helping calcium and vitamin D3 build strong bones when we are young, and slowing the natural effects of aging on bones and heart in later years.*

Unprotected K2 MK-7 is not stable when combined with calcium or magnesium. *A five-year ongoing analysis by Kappa Bioscience demonstrates this conclusion, most recently in this K2 Market Study 2017.*

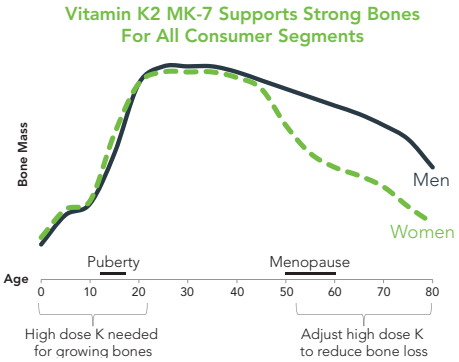
Calcium and magnesium are at the core of many bone, heart and multivitamin product formulations. *This should prohibit the use of unprotected K2 in these products, as well as in products in other categories that also use minerals, like women's health and anti-aging. The 2017 testing results, however, demonstrate that too many K2 products on the market are still failing, despite growing awareness and market discussion of unprotected K2 stability.*

A minority of 2017 K2-plus-minerals products tested met K2 label claim. Two-thirds missed label claim by over 50%. One-in-three products contained zero K2. *While in 2017 some leading K2 companies acknowledged and responded to the K2 stability problem, testing demonstrates that many segments of the market continue to fall short.*

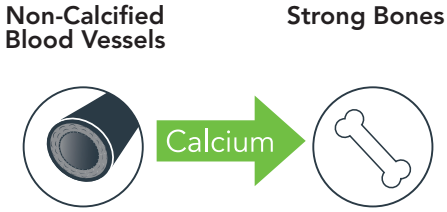
Kappa Bioscience solved the K2-plus-minerals stability problem with protected, microencapsulated K2VITAL® DELTA. *Over 3 years stability testing and 100's of stable products in the market assure DELTA® stability. This K2 Market Study presents 5 years of data, including a 2017 update of 119 finished products that were collected globally and analyzed for K2 label claim.*

K2VITAL® DELTA

K2 OVERVIEW:
K2 STABILITY POSES A CHALLENGE IN MAJOR MARKET CATEGORIES



Vitamin K2 is an essential fat-soluble vitamin. K2 activates osteocalcin proteins which incorporate calcium into bone. The MK-7 form of K2 is optimal for dietary supplementation because a half-life of 2-3 days provides better absorption compared to MK-4 (2 hours) [1, 2]. Bone health in childhood and adolescence improves the outlook for bone health later in life. Strong, dense bones in adulthood help avoid fractures and bone disease like osteoporosis. Peak bone mass (PBM) is reached around the age of 13-19 years [3] followed by declines throughout adult life, especially for women. A 10% increase in PBM by age 20 is estimated to reduce the risk of osteoporotic fracture later in life by 50% [4].



Vitamin K2 also activates matrix GLA proteins (MGP), which bind excess calcium in blood to prevent deposit in arteries and vessels – a risk factor for cardiovascular disease [5] and common condition as we age. High levels of vitamin K2 are found in the Japanese dish natto and some fermented cheeses, but most western diets are K2-deficient [6]. Vitamin K2 needs to be supplemented.

Unprotected K2 MK-7, like other fat-soluble vitamins, can degrade in certain environments and formulations. Vitamin K2 is sensitive to alkaline environments such as in formulation with minerals. Finished products containing unprotected K2 and minerals have a high probability of missing K2 label claim and falling short on promises to brands and consumers. This effectively blocks the use of unprotected K2 in bone and heart health products because calcium and magnesium are core ingredients in these categories. Other market categories are similarly affected, including multivitamin, women's health, and sports nutrition. Because unprotected K2 is unstable, and overage in manufacturing is not an economical solution, the use of vitamin K2 MK-7 in these categories is limited without a solution. Unprotected K2-plus-minerals products should not be put on the market.

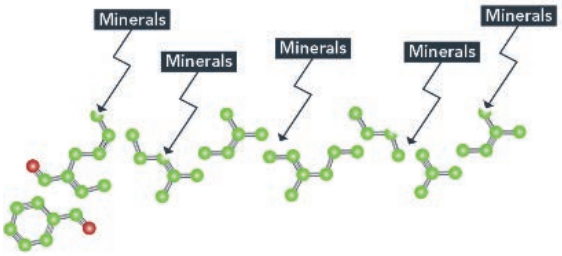
VITAMIN K2 MK-7 IS A FAT SOLUBLE VITAMIN. It can degrade in certain environments and formulations.

K2VITAL® DELTA

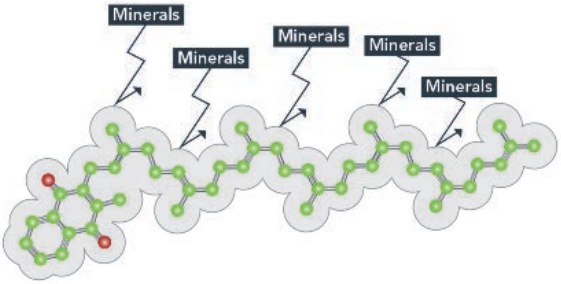
Kappa Bioscience solved K2 stability-with-minerals with the development of protected, microencapsulated K2VITAL® DELTA. The DELTA® double-coated, spray-dried beadlet contains minimal trapped air, promoting K2 stability from within and without. With DELTA®, Kappa Bioscience opened market categories that were otherwise closed to the benefits and opportunity of K2 MK-7.

The development and launch of DELTA® was based on a testing program of K2 products available in the market and sold to consumers – a program now it its sixth year. This K2 Market Study represents the 2017 results of nearly 120 label claim tests conducted on K2 products purchased from retailer shelves globally.

Unprotected Vitamin K2



K2VITAL® DELTA



KAPPA BIOSCIENCE SOLVED K2 STABILITY-WITH-MINERALS with the development of protected, microencapsulated **K2VITAL® DELTA.**

K2VITAL® DELTA

STUDY BACKGROUND:
DISCOVERY OF A STABILITY PROBLEM

In 2012 Kappa Bioscience launched K2VITAL® vitamin K2 MK-7. K2VITAL® was the first vitamin K2 manufactured by organic synthesis, compared to the more common fermentation production method. In 2013 Kappa began a K2 analysis program by testing 101 vitamin K2 products for stability or label claim. Four-of-five products (81%) did not meet label claim, including some K2VITAL® products.

Kappa began an intensive R&D program to identify and solve the problem. Investigations eventually pointed to a fundamental property of vitamin K2. As a fat-soluble vitamin, and similar to all fat-soluble vitamins, unprotected vitamin K2 can degrade in certain environments and formulations. K2 is particularly susceptible to degradation in formulation with minerals and in other harsh alkaline environments, such as with krill or L-arginine.

To solve K2 instability Kappa developed a protected, microencapsulated vitamin K2 MK-7 form with a unique two-layered coating. This form provides high-quality and stable vitamin K2 MK-7, with good flow and handling abilities compared to fermented K2. The compact beadlet enables DELTA® to deliver provable stability with less overage in manufacturing. Calcium, magnesium and multivitamin products that contain DELTA® will have a longer shelf-life, ensuring that products meet label claim.

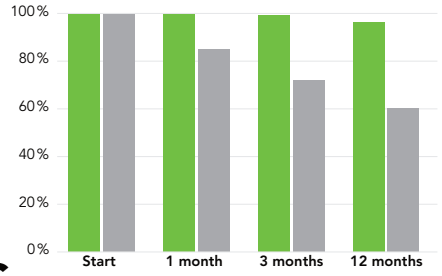
K2VITAL® DELTA demonstrated minimal loss in assay over a 12-month period at both normal and accelerated temperatures (25°C and 40°C). In comparison, unprotected K2 MK-7 showed very significant decreases of MK-7 under the same conditions with both calcium and magnesium. *(see figures 1-4)*

Calcium, magnesium and multivitamin products that contain DELTA® will have a longer shelf-life, ensuring that products meet label claim.

K2VITAL® DELTA

Figure 1

Vitamin K2 MK-7 with Calcium carbonate



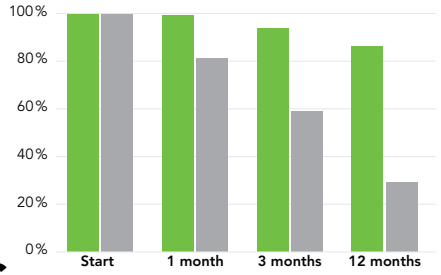
25°C

K2VITAL® DELTA	100 %	100 %	99 %	96 %
Fermented K2 powder	100 %	85 %	72 %	60 %

Source: Synthetica AS © Kappa Bioscience 2017

Figure 2

Vitamin K2 MK-7 with Calcium carbonate



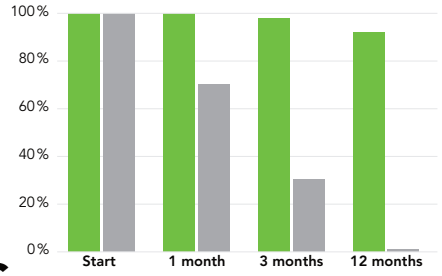
40°C

K2VITAL® DELTA	100 %	99 %	94 %	86 %
Fermented K2 powder	100 %	81 %	58 %	29 %

Source: Synthetica AS © Kappa Bioscience 2017

Figure 3

Vitamin K2 MK-7 with Magnesium oxide



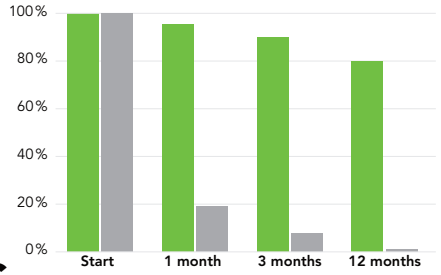
25°C

K2VITAL® DELTA	100 %	100 %	98 %	92 %
Fermented K2 powder	100 %	70 %	30 %	1 %

Source: Synthetica AS © Kappa Bioscience 2017

Figure 4

Vitamin K2 MK-7 with Magnesium oxide



40°C

K2VITAL® DELTA	100 %	95 %	89 %	80 %
Fermented K2 powder	100 %	19 %	8 %	1 %

Source: Synthetica AS © Kappa Bioscience 2017

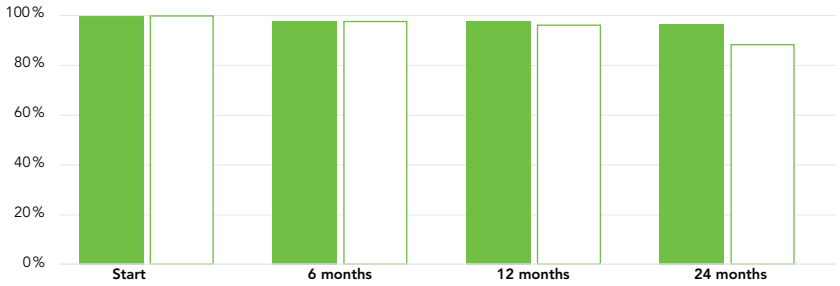
K2VITAL® DELTA DEMONSTRATED MINIMAL LOSS.
In comparison, **unprotected K2 MK-7 showed very significant decreases of MK-7** under the same conditions.

K2VITAL® DELTA

K2VITAL® DELTA offers the assurance of stability with over 2 years of long-term stability testing, demonstrating minimal loss of K2 even at accelerated temperatures. *(see figure 5)*

Figure 5

DELTA® Encapsulated K2 MK-7 Stability



25°C
40°C

K2 MK-7 / 25°C	100 %	98 %	98 %	97 %
K2 MK-7 / 40°C	100 %	98 %	96 %	89 %

Source: Synthetica AS © Kappa Bioscience 2017

Note: Testing standard deviation +/- 3 % for 24 months at 40° C

Over a period of 24 months K2VITAL® DELTA demonstrated minimal loss at both normal and accelerated temperatures (25°C and 40°C).

K2VITAL® DELTA

MARKET STUDY:
K2 STABILITY/LABEL CLAIM IN FINISHED PRODUCTS – 2017 UPDATE

STUDY OBJECTIVES AND SAMPLING

Rapid K2 market growth, new awareness of K2 stability, and increasing attention to quality and consumer protection set the stage for Kappa Bioscience to update its ongoing vitamin K2 Market Study. From the period of January to December 2017 Kappa conducted assay tests for label claim on 119 vitamin K2 products purchased globally from retailers and online.

Products were sourced globally, with strong representation of major K2 markets such as the N. America, EU and Australia, plus representation from Asia, South America, Middle East and Africa. Dosage forms primarily included tablets, capsules, chewable tablets, gums and liquids. Date of both manufacture and expiry were recorded as available, and all products tested were in the first or second quartile of the expiration period. The 2017 sampling focused on K2-plus-mineral formulations and K2 alone or in non-mineral formulations. No sample stratification by market, producer, brand or any other variable was attempted.

In Q4 2017 Kappa launched a free K2 product testing program, with an offer to test K2 products from any source for K2 content (with some qualifications). Products received from this program represent approximately 10% of the total sample.

The final sample consisted of 119 finished K2 products, which were identified among all Kappa 2017 tests after removal of duplicate tests, and R&D tests used for method develop for testing new dosage formats.

STUDY METHODOLOGY

Assay was completed utilizing a validated HPLC method for the testing of K2 MK-7. The general principle of the method is determination of MK-7 by HPLC with UV detection at 270 nm, and external standard calibration. MK-7 is released from the matrix by a process of adding water/ethanol to the product, followed by extraction of the vitamin in ethyl acetate. Assay was compared to labeled claim of K2 content within the individual product. Testing was conducted by Synthetica AS, a leader in the preparation and analysis of fat-soluble vitamins and producer and provider of K2 MK-7 reference samples, including as vendor of record for reference samples to the USP. A sub-sample of 5% of tests were cross-validated by an independent, third-party testing laboratory.

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STUDY FINDINGS

UNPROTECTED/FERMENTED K2 MK-7 PLUS CALCIUM OR MAGNESIUM

In total, 103 finished products containing vitamin K2 MK-7 plus calcium or magnesium (various forms) or K2 MK-7 in a multivitamin formulation were tested. Of these, 94 products used unprotected or fermentation-produced K2 MK-7.

Only 9% of these products met product label claim within a margin of three percent. Sixteen percent missed K2 label claim by 75% to 87%. About one-in-five products (19%) missed label claim by 50% to 74%.

Two-thirds (62%) of all unprotected K2 plus calcium, magnesium or minerals products missed label claim by 50% or more. This includes 15% of all products which measured 26% to 50% of K2 label claim, and 15% which demonstrated between 1 to 24% label claim.

One-in-three products (32%) tested contained zero K2, with testing demonstrating no measurable K2 content. These 2017 findings demonstrate either a worsening of the problem compared to the previous year (where half of products missed by 50% or more and 10% contained zero K2) or that the 2016 sampling failed to measure the full scope of the problem. *(see figures 6a and 6b)*

Two-thirds (62%) of all unprotected K2 missed label claim by 50% or more. One-in-three products (32%) tested contained zero K2, with testing demonstrating no measurable K2 content.

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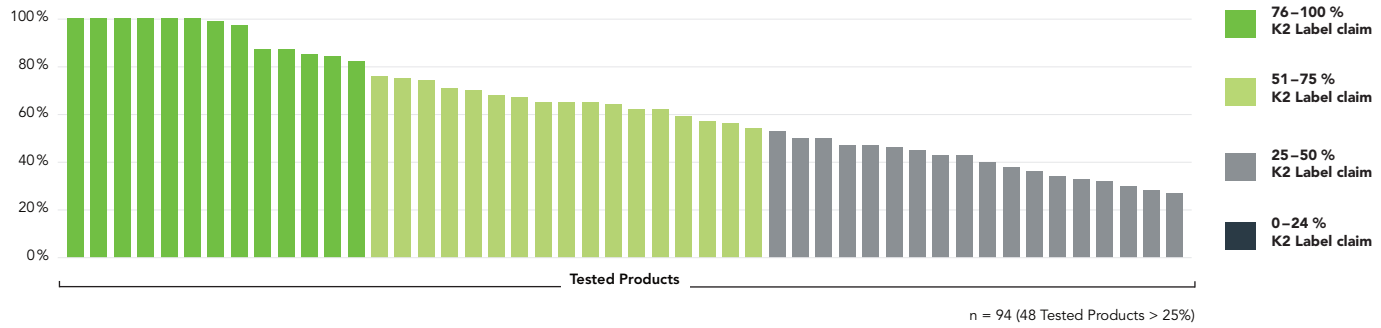
CHART 1 OF 2

Figure 6a

Percent Label Claim: Unprotected/Fermented K2 plus Calcium or Magnesium Finished Products

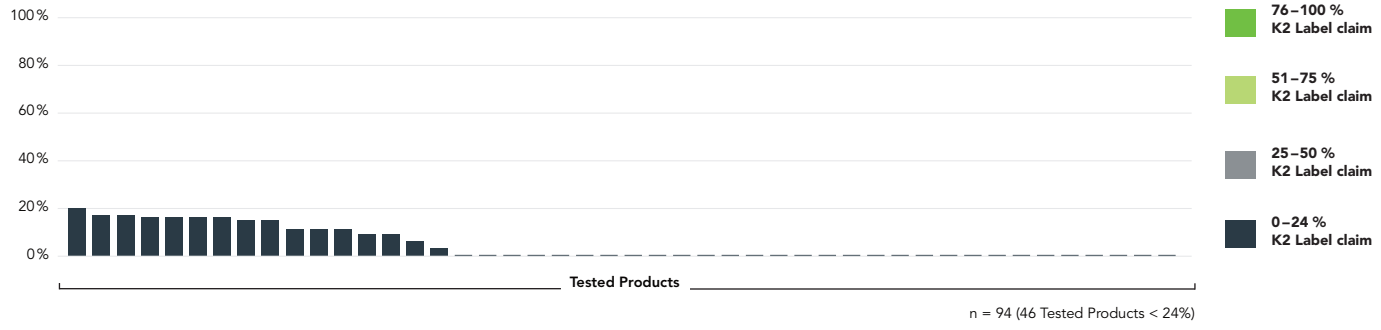


n = 94 (48 Tested Products > 25%)

CHART 2 OF 2

Figure 6b

Percent Label Claim: Unprotected/Fermented K2 plus Calcium or Magnesium Finished Products



n = 94 (46 Tested Products < 24%)

Only 8 of 94 unprotected K2 plus calcium, magnesium or minerals products **met label claim.**

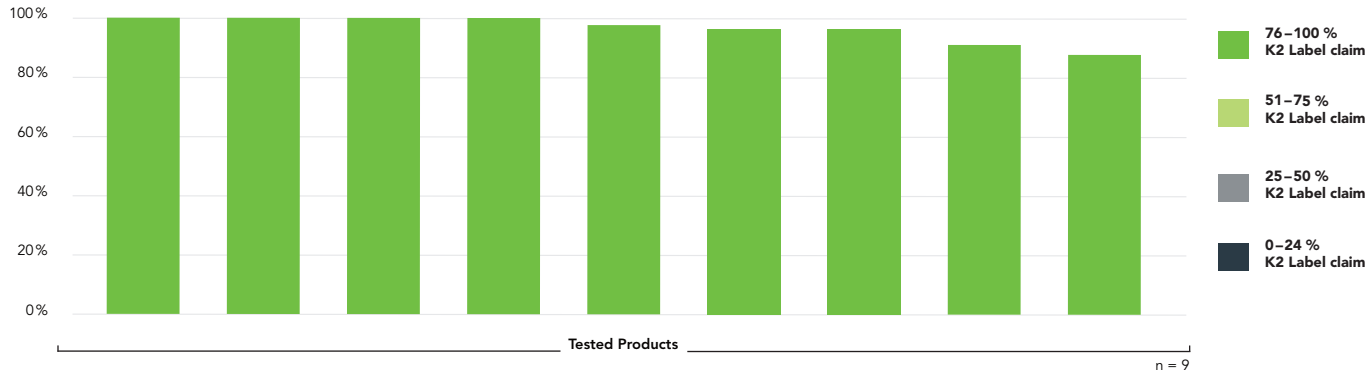
K2VITAL® DELTA

PROTECTED, MICROENCAPSULATED K2VITAL® DELTA PLUS CALCIUM OR MAGNESIUM

Of the 103 K2-plus-minerals tests conducted, 9 contained protected K2VITAL® DELTA. These 2017 DELTA® products performed strongly, with all but two meeting label claim within a margin of 3 percentage points, and the remainder performing in the 90% range, within USP monograph definitions. These results generally mirror the 2016 results which also demonstrated strong DELTA® performance. *(see figure 7)*

Figure 7

Percent Label Claim: K2VITAL® DELTA plus Calcium or Magnesium Finished Products 2017



K2VITAL® DELTA

UNPROTECTED/FERMENTED K2 MK-7 ALONE OR IN NON-MINERAL FORMULATIONS

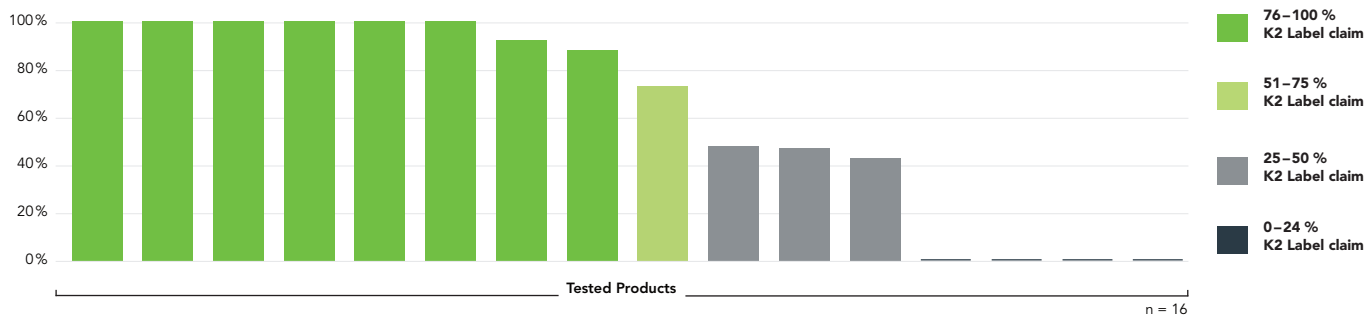
The 2016 study produced an unexpected finding, specifically that over half of K2-alone or K2 plus non-mineral product formulations performed poorly, with one-in-three products demonstrating no measurable K2 content (zero). Mono-K2 and non-mineral multi-ingredient formulations should pose no problem for K2 stability.

While the 2017 sample of these non-mineral products was smaller than the previous year by half, the results demonstrated some improvement. Over a third (38%) of these products met label claim, up from 27% in 2016. A quarter (25%) contained zero K2, which was down from 33% in 2016.

However, further analysis of the 2016 findings demonstrated that poor results were correlated with K2 from Chinese origin. The hypothesis was that low K2 amounts were due to poor K2 ingredient quality and not improper ingredient handling during manufacture. Subsequent 2016 tests provided support for this theory, as several of the Chinese-origin products demonstrated high *cis* levels (non-bioactive MK-7) indicating problems stemming from ingredient manufacture. The 2017 sample did not include a similar proportion of Chinese-origin products, and as such a year-on-year comparison should be viewed as inconclusive. *(see figure 8)*

Figure 8

Percent Label Claim: Unprotected/Fermented K2 MK-7 Alone or in Non-mineral Formulations



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UNPROTECTED/FERMENTED K2 MK-7 PLUS CALCUIM OR MAGNESIUM: ONLINE RETAILER SUBSET

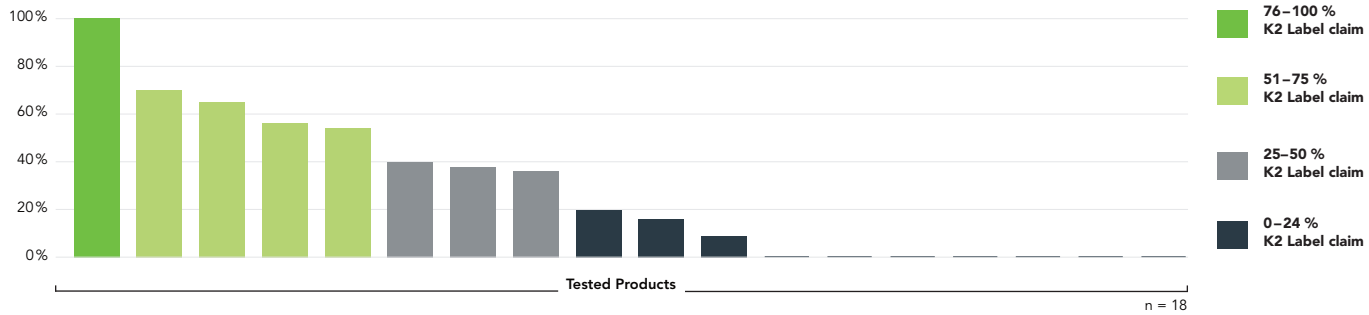
The importance of online channels for consumer purchase of dietary supplements continues to grow, with perhaps as many as half of all products purchased online. To test the quality of K2 products available online Kappa created a 2017 subsample of products purchased online.

On a single day, August 2, 2017, Kappa purchased all unprotected K2-plus-minerals products available via Amazon.com, with available shipping within the US. In total, 18 products were purchased and tested – products primarily marketed in the bone or heart health categories, plus several multivitamins.

Only one of these products met label claim. About 1 in 5 (22%) missed label claim by 50 to 70%. Two-thirds (66%) missed label claim by over 50%. In total, nearly forty percent (39%) of unprotected K2-plus-minerals products purchased online on a given day contained zero K2. *(see figure 9)*

Figure 9

Percent Label Claim: Unprotected/Fermented K2-Plus-Minerals Ordered on a Single Day



7 of 18 products purchased online contained zero K2. Only one product met label claim.

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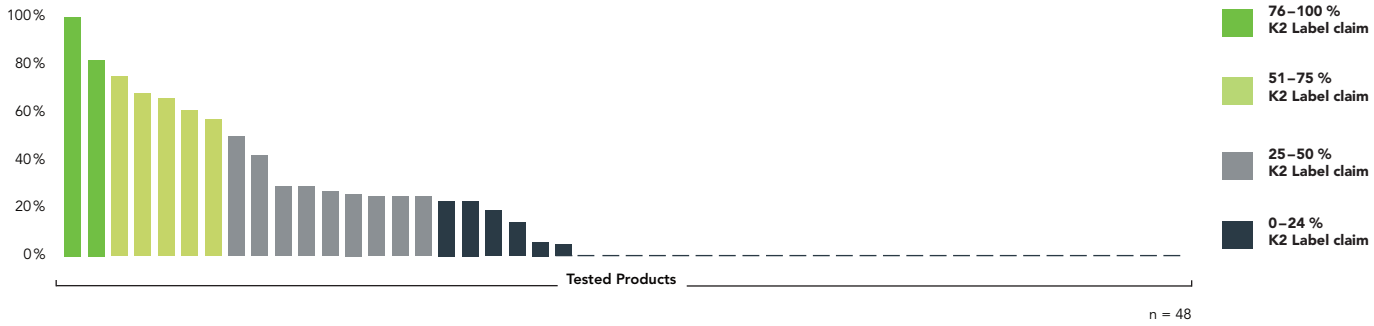
UNPROTECTED/FERMENTED K2 MK-7 ALONE OR IN NON-MINERAL FORMULATIONS: ONLINE RETAILER SUBSET 2

A single-day order provides a spot check, but is not necessarily representative of the online marketplace. To verify 'online findings', Kappa analyzed all K2 products purchased on Amazon between 2016 to April 2018, with delivery to EU, and excluding the single-day test products. Products were primarily K2-alone or non-mineral formulations (98%). In total 48 products were reviewed. Sampling was biased towards 'low price' products where it was estimated that the cost-per-daily-dosage of the raw K2 ingredient would exceed the price of the product's daily dosage (based on industry-wide estimates of K2 manufacturing costs).

Figure 10

Percent Label Claim: Unprotected/Fermented K2 Products Ordered Online (2016-2018)
Effective Label Claim (Label Claim minus *cis*/Inactive MK-7 %)



Only 9 of 48 products (19%) met the USP monograph assay requirements with 90% or more of stated label claim. Over half (54%) contained zero K2, and most of the rest measured 50% or less K2 label claim. The relatively good performance of the 9 products, however, proved misleading.

Follow-up analysis demonstrated that only 1 of 48 products (2%) met the Effective Label Claim for biologically active MK-7. Fully 98% did not meet this measure as they either missed assay for MK-7 or included high levels of biologically inactive *cis* MK-7. *(see figure 10)*

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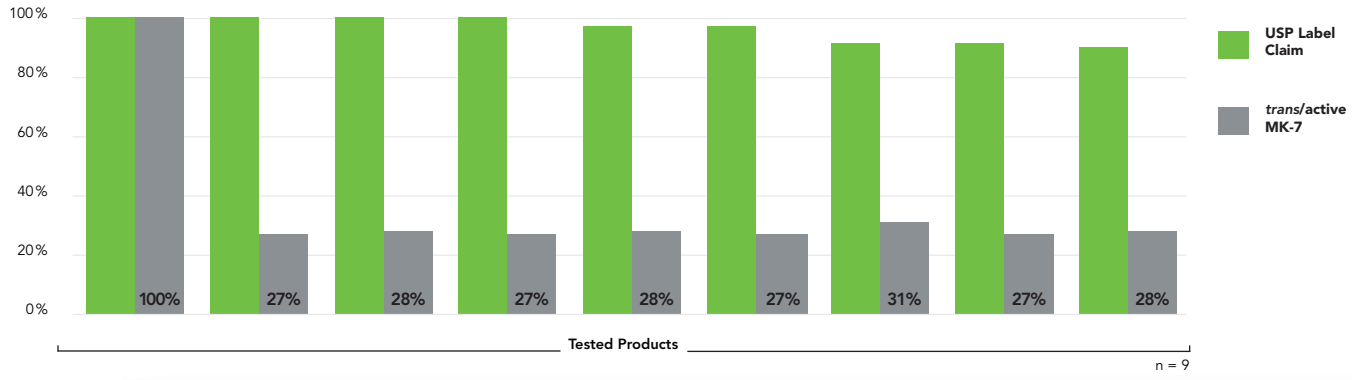
Effective Label Claim was calculated by conducting a second test, USP 38NF33 for isometric purity, on the 22 products that demonstrated some MK-7 (3µg to 305µg). Only 4 of these products contained 100% all-*trans* biologically-active MK-7, but only 1 also met assay requirements for MK-7 amount (e.g. met Effective Label Claim.). In total, only one product of 48 met Effective Label Claim of MK-7 amount minus *cis*/biologically-inactive MK-7.

Of the nine products that met the USP assay label claim requirements of >90% MK-7, eight contained nearly 75% (average) *cis*/biologically-inactive MK-7. These products would deliver the biological equivalent of 25% of the stated MK-7 label claim. *(see figure 11)*

Figure 11

Percent Label Claim: Unprotected/Fermented K2 Products Ordered Online (2016-2018)
USP Label Claim vs. *trans*/Active MK-7



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Conclusions

Like all fat-soluble vitamins, K2 MK-7 can degrade in certain environments and formulations. K2 is particularly susceptible to degradation in formulation with calcium or magnesium. Unprotected vitamin K2 in calcium, magnesium or high-alkaline formulations will degrade, with a high probability that finished consumers products will not meet K2 label claim - likely by a wide margin.

Calcium is a primary co-ingredient in bone health formulations, magnesium is a primary co-ingredient in heart health formulations. Without a solution, unprotected K2 MK-7 is blocked from use in market categories that leverage calcium or magnesium, including the bone, heart, multivitamin, women's health and anti-aging health categories.

A subset of K2 MK-7 manufactures are not producing a quality ingredient. With two-thirds of K2-plus-minerals products and one-third of mono-K2 products containing zero K2, the rapidly expanding K2 market clearly includes some low-quality producers. Quality manufactures must educate brands about K2 formulation limitations, and brands should require transparency of documentation and increased testing of finished products.

While this 2017 Market Study update demonstrates expected (poor) results for unprotected K2-plus-minerals formulations, comparisons to 2016 demonstrate either a worsening situation or that the full scope of the problem has yet to be fully defined. Despite an increase in industry awareness and discussion of K2-plus-minerals stability, and K2 market acknowledgement of the problem (as demonstrated by the market introduction of two additional K2 ingredient products that target stability), a higher percentage of products sold to consumers contain low or zero levels of K2.

Microencapsulated K2VITAL® DELTA from Kappa Bioscience solved the K2-plus-minerals stability problem. Five years of testing demonstrates the performance of DELTA® compared to unprotected/fermented K2 MK-7. With DELTA® Kappa opens previously closed or restricted market categories to the benefits of vitamin K2 MK-7. This applies to the bone and heart health categories, as well as all other categories that frequently leverage calcium or magnesium. DELTA® assures K2 quality, performance and meeting promised made to consumers.

References
1. Moller, M., et al., *Bioavailability and Chemical/Functional Aspects of Synthetic MK-7 vs Fermentation-Derived MK-7 in Randomised Controlled Trials.* Int J Vitam Nutr Res, 2016: p. 1-15.
2. Schurgers, L.J., et al., *Vitamin K-containing dietary supplements: comparison of synthetic vitamin K1 and natto-derived menaquinone-7.* Blood, 2007. **109**(8): p. 3279-83.
3. Bailey, D.A., R.A. Faulkner, and H.A. McKay, *Growth, physical activity, and bone mineral acquisition.* Exerc Sport Sci Rev, 1996. **24**: p. 233-66.
4. Bailey, D.A., *The Saskatchewan Pediatric Bone Mineral Accrual Study: bone mineral acquisition during the growing years.* Int J Sports Med, 1997. **18 Suppl 3**: p. S191-4.
5. Schurgers, L.J., J. Uitto, and C.P. Reutelingsperger, *Vitamin K-dependent carboxylation of matrix Gla-protein: a crucial switch to control ectopic mineralization.* Trends Mol Med, 2013. **19**(4): p. 217-26.
6. Cundiff, D.K. and P.S. Agutter, *Cardiovascular Disease Death Before Age 65 in 168 Countries Correlated Statistically with Biometrics, Socioeconomic Status, Tobacco, Gender, Exercise, Macronutrients, and Vitamin K.* Cureus, 2016. **8**(8): p. e748.

K2VITAL® DELTA

K2VITAL® DELTA from Kappa Bioscience is the only vitamin K2 that meets the requirements of finished products that contain either calcium or magnesium. DELTA® contains pure all-*trans* K2 MK-7, ensuring your product meets its K2 label claim.

Test protocols are available upon request: **Kappa would be happy to help you evaluate DELTA® by confidentially testing your current K2-plus-minerals products.**

K2VITAL® DELTA, the new standard in vitamin K2 MK-7.

Contact the specialists at Kappa Bioscience to learn more about K2VITAL® DELTA and vitamin K2 stability.

Kappa Bioscience is the pioneer in development and production of the only synthetic and biologically active all-*trans* menaquinone-7 (vitamin K2 MK-7), marketed under the K2VITAL® brand name.

Kappa's innovation of MK-7 synthesis marks the commercial milestone where this fat-soluble vitamin can begin to attain widespread consumer adoption. Effective synthesis production drives scalability, price reduction and a secure supply chain - with unmatched ingredient purity and documentation.

Combined with other Kappa innovations such as the patented DELTA® microencapsulation process, which provides K2 stability in mineral formulations, K2VITAL® offers brands and manufacturers a path to broader market segments.

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