

## **Vitamin K**

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### *Function*

Vitamin K<sub>1</sub>, or phylloquinone, regulates the synthesis of blood-clotting proteins and the organic matrix of bone; it is obtained from the diet and is produced by the intestinal microflora (Food and Nutrition Board 2001; Olson 1999). Phytonadione is the name given to common pharmaceutical preparations of vitamin K<sub>1</sub>. The extent to which vitamin K synthesis by intestinal bacteria contributes to vitamin K status requires further investigation. Vitamin K deficiency due to dietary inadequacy is rare or nonexistent in healthy adults, but may be found in some adults with fat-malabsorption syndrome. In breast-fed newborns, vitamin K deficiency represents a significant health problem. It is by antagonizing vitamin K activity that coumarin drugs decrease the risk of unwanted blood clotting involved in thrombotic stroke and heart disease.

### **Safety Evidence**

There are no reports of toxic effects from vitamin K as vitamin K<sub>1</sub> (phylloquinone/phytonadione, the form in conventional foods and dietary supplements) (Food and Nutrition Board 2001), even at 500 times the RDA (Olson 1999). Menadione, a synthetic derivative of vitamin K that is marketed in a water-soluble form for use in animal feeds, can cause adverse effects when injected (Olson 1999). With phylloquinone, no adverse effects have been observed in persons who have ingested large amounts over long periods of time (Food and Nutrition Board 2001). Because of the antagonistic interaction between vitamin K and coumarin drugs, persons taking coumarin drugs should not significantly change their dietary or supplementary vitamin K intake without first informing their physicians. Similarly, vitamin K activity and clotting functions must be carefully considered before oral antibiotics are prescribed for patients taking coumarin drugs.

### **Published Official Reviews of Vitamin K Safety**

The FNB found no reports of adverse effects for vitamin K as phylloquinone; hence, it concluded that there was no basis for a LOAEL or a NOAEL value (Food and Nutrition Board 2001). Lacking a LOAEL or a NOAEL, no UL value was established.

The EC SCF recognized (Scientific Committee on Food 2003) that no adverse effects occurred in a small, short-term clinical trial of 10 mg of phylloquinone per day (Craciun et al. 1998). Given these findings, EC SCF did not set a UL value.

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The UK EVM cited that same study as evidence of a lack of adverse effect at 10 mg of phylloquinone per day. Because of the small size of that trial, UK EVM selected a UF of 10 to correct for potential inter-individual variation and therefore calculated a GL of 1 mg per day (1,000 µg per day) (Expert Group on Vitamins and Minerals 2003).

## **CRN ULS (OSL Method) for Vitamin K**

Vitamin K has an extremely low potential for toxicity, but the data are insufficient to establish just how low. The UK EVM's decision to apply a UF of 10 seems unnecessarily cautious in view of the absence of reports of adverse effects at intakes of 30 mg or more, although data to support the 30 mg value are sparse. Consequently, CRN identifies the ULS for vitamin K as 10 mg per day. This value is based on the same clinical data identified by UK EVM (Craciun et al. 1998) but without the tenfold UF. Using a factor of 1 instead of 10 is justified by the apparent absence of adverse effects at intakes of 30 mg or more. Dietary intake and intestinal biosynthesis are trivial in comparison with the ULS of 10 mg.

Because of the strong interaction of vitamin K with anticoagulant drugs, the ULS does not apply to persons taking such medications.

<b><u>Comparison of Safety Values for Vitamin K</u></b>	
<b>CRN ULS (OSL method)</b>	10 mg
<b>US FNB UL</b>	Reviewed but not established (no toxicological basis)
<b>EC SCF UL</b>	Reviewed but not established (no toxicological basis)
<b>EC supplement maximum</b>	Not established (as of May 2004)
<b>UK EVM GL, supplement</b>	1 mg (1,000 µg) (10 mg ÷ 10)

## *References*

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