are enzymatic, such as: (1) superoxide dismutase enzymes, which remove superoxide ($O_2^{\cdot -}$) by accelerating its conversion to H_2O_2 and O_2; (2) glutathione peroxidases, which convert H_2O_2 to water and O_2 and which convert various hydroperoxides to harmless compounds; and (3) catalase, which converts H_2O_2 to water and O_2 but only functions at relatively high concentrations of the ROS.

Evidence for Antioxidant Activity

Many substances have been shown to have antioxidant activity *in vitro*. However, *in vitro* findings are of uncertain relevance to the *in vivo* situation in healthy humans. The definition of a dietary antioxidant focuses on antioxidant effects of substances when consumed by humans. Therefore, dietary antioxidants are substances that have been shown to decrease the effects of ROS and RNS in humans.

A battery of markers of *in vivo* oxidative damage/oxidative stress are now available. Potential biomarkers include (1) lipid peroxidation products, such as lipid hydroperoxides, malondialdehyde or other aldehydic decomposition products of lipid hydroperoxides, exhaled pentane and ethane, and F_2-isoprostanes; (2) several DNA oxidation products such as 8-oxo-deoxyguanosine, 8-oxydeoxyadenosine, and thymine glycol; (3) protein carbonyls; and (4) nitrated protein derivatives.

FOOD COMPONENTS THAT WILL BE REVIEWED BY THE PANEL

This section contains a description of the scope of the second report of the Panel on Dietary Antioxidants and Related Compounds. The panel has focused on nutrients and food components found in North American diets because the objective of the second report of this panel is to present a set of DRIs for promotion and maintenance of health in Americans and Canadians. The inclusion of substances is not based upon the requirement that they meet the proposed definition of a dietary antioxidant. Although there may be some functional relationship to their proposed roles as antioxidants, their inclusion in the second report is not based upon their meeting this criterion. The panel plans to review beta-carotene and other carotenoids, vitamin C, vitamin E, and selenium. The rationale for including these food components but not other potential substances follows.

Beta-Carotene and Other Carotenoids

Beta-carotene and other carotenoids—such as alpha-carotene, lycopene, lutein and zeaxanthin, and cryptoxanthin—are widely consumed in human diets, and adequate food composition data exist to estimate their consumption in

healthy people. Studies demonstrating the possible antioxidant effects of carotenoids in humans are available, at least with regard to beta-carotene, as are a large number of observational studies associating carotenoid intake or carotenoid status with a variety of health effects. In addition, some experimental studies of beta-carotene in humans are also available. Thus, an examination of the scientific evidence regarding beta-carotene and other carotenoids is warranted. The panel will review the available scientific evidence and, if it is adequate, will recommend DRIs for beta-carotene and possibly other carotenoids.

Vitamin C

Vitamin C is found in abundance in fruits and vegetables. It is a cofactor in the biosynthesis of a number of different compounds including collagen, carnitine, and neurotransmitters. In addition, because it can donate electrons, it effectively quenches a variety of ROS and RNS in aqueous body compartments, and it has been shown in some cases to prevent oxidative damage *in vivo* to lipids and DNA. Under certain circumstances, vitamin C can promote the formation of ROS or RNS *in vitro*. Vitamin C is found widely throughout the body and is concentrated in tissues susceptible to oxidative damage including leukocytes, the lung, eye, brain, and heart. It is readily regenerated *in vitro,* and because of its high reductive capacity, has the potential ability to regenerate other body antioxidants. Vitamin C's role in preventing scurvy is relatively well defined and is distinct from its role in oxidant defense. A great deal of observational and experimental evidence is available regarding vitamin C's health effects. Thus, the panel will review the available scientific data and, if it is adequate, will establish DRIs for vitamin C.

Vitamin E

Vitamin E is composed of a group of fat-soluble molecules that occur naturally in eight different forms (four tocopherols and four tocotrienols) that have similar chromanol structures. It occurs widely in the diet from both plant and animal sources, and adequate food composition data are available. Vitamin E has been demonstrated to possess antioxidant activity *in vivo* and can protect unsaturated lipids throughout the body. Under certain circumstances, vitamin E can act as a prooxidant *in vitro*. In addition, there is epidemiological and experimental evidence regarding the health-promoting effects of vitamin E. Thus, the panel will review the available scientific data and, if it is adequate, will establish DRIs for vitamin E.