10. Evaluation

10.1 Cancer-preventive activity

10.1.1 Humans

There is *evidence suggesting lack of cancer-preventive activity* for β-carotene when used as a supplement at high doses. There is *inadequate evidence* with regard to the cancer-preventive activity of β-carotene at the usual dietary levels. There is *inadequate evidence* with respect to the possible cancer-preventive activity of other individual carotenoids.

10.1.2 Experimental animals

There is *sufficient evidence for cancer-preventive activity* of β-carotene in experimental animals. This evaluation is based on models of skin carcinogenesis in mice and buccal pouch carcinogenesis in hamsters. Findings in models of liver carcinogenesis in rats, colon carcinogenesis in rats and pancreatic carcinogenesis in rats and hamsters provide further support to this conclusion.

There is *sufficient evidence for cancer-preventive activity* of canthaxanthin in experimental animals. This evaluation is based on models of skin carcinogenesis in mice and buccal pouch carcinogenesis in hamsters. Findings in models of tongue cancer in rats and stomach carcinogenesis in mice provide additional support to this conclusion.

There is *limited evidence* that α-carotene has cancer-preventive activity from single studies of models of liver, lung, skin and colon carcinogenesis. There is *limited evidence* that lycopene has cancer-preventive activity from models of colon, liver, mammary gland and lung carcinogenesis. There is *limited evidence* that lutein has cancer-preventive activity from experimental models of colon and skin carcinogenesis. There is *limited evidence* that fucoxanthin has cancer-preventive activity from models of skin and duodenal carcinogenesis.

10.2 Overall evaluation

The results of studies in experimental animals and clinical studies in humans with regard to the cancer-preventive activity of β-carotene are conflicting. There is sufficient evidence that β-carotene has cancer-preventive activity against cancers of the skin and buccal pouch in experimental animals, supported by the results of studies in models of cancer of the liver, colon and pancreas. Moreover, there is considerable in-vitro and in-vivo evidence in animals that β-carotene inhibits the induction or expression of cancer-related events.

In observational epidemiological studies, β-carotene in blood or in the diet has been associated with reduced risks for cancers at many but not all sites. It is unclear, however, to what extent β-carotene itself is responsible for the decreased risks observed. Three large clinical trials indicate that supplementation with substantial doses of β-carotene does not prevent lung cancer and may actually increase the risk

among individuals already at high risk (i.e. who are cigarette smokers or who have been occupationally exposed to asbestos). Although β-carotene is not known to be toxic in the short term, the intervention trials also suggest increased risks for cardiovascular death after supplementation. These trials do not provide clear evidence concerning cancers at specific sites other than the lung.

The discrepancies between the experimental and human observations and the findings from the intervention trials greatly complicate interpretation of the data on the effects of β-carotene. Understanding these discrepancies is an important aim of future research. Such investigation is also likely to provide insight into the process of carcinogenesis and increase knowledge about cancer prevention. Until such clarification is obtained, β-carotene supplements should not be recommended for use in cancer prevention in the general population and it should not be assumed that β-carotene is responsible for the cancer-protective effects of diets rich in carotenoid-containing fruits and vegetables.

Other carotenoids, canthaxanthin, α-carotene, lutein, lycopene and β-cryptoxanthin, have been investigated *in vitro* and in animal models, although not as extensively as β-carotene. There is *sufficient evidence* that canthaxanthin has cancer-preventive activity in animal models of cancers of the skin and buccal pouch, supported by the results of studies in models of cancers of the tongue and stomach. There is *limited evidence* that α-carotene, lycopene, lutein and fucoxanthin have cancer-preventive activity in a variety of animal models. Canthaxanthin inhibits the expression of cancer-related events *in vitro*.

The results of observational epidemiological for α-carotene, lycopene and lutein are much less extensive than those for β-carotene; no published results are available for canthaxanthin,. These carotenoids have not been studied in human trials for cancer prevention. Pending further research into their cancer-preventive activity, supplemental canthaxanthin, α-carotene, lutein and lycopene should not be recommended for use in cancer prevention in the general population, and it should not be assumed that the protective effects of diets rich in carotenoid-containing fruits and vegetables are due to any individual carotenoid.