Lay Summary of the Statement on the effects of excess Vitamin A on maternal health

1 In 2019, The Scientific Advisory Committee on Nutrition (SACN) agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery; this would include the effects of chemical contaminants and excess nutrients in the diet. The Committee on Toxicity was consulted, and decided that Vitamin A should be considered for assessment of the risks associated with excess intake.

2 Vitamin A (also called retinol) is found in foods of animal origin (such as liver, paté and cod liver oil) and is also formed in the body when beta-carotene – the colouring matter in red and yellow, and leafy green vegetables – is broken down. The NHS.uk website lists significant food sources of vitamin A as cheese, eggs, oily fish, fortified low-fat spreads, milk, yoghurt and liver and liver products such as paté. Significant sources of beta-carotene include certain vegetables such as carrots, sweet potatoes, red peppers and spinach, and some fruit such as mango, papaya and apricots.

3 Retinol is changed, after it is eaten, into other chemical forms that are involved in several biological functions, such as the proper growth of the fetus in pregnancy (in a form called retinoic acid) and how the retina in the eye senses light (in a form called retinal). Most of the effects of vitamin A are caused by retinoic acid, which, among other things, influences bone development and secretion of hormones from the thyroid gland, and stimulates the immune system improving resistance to infections. Different chemical forms of vitamin A and synthetic substances that mimic it are also used as medicines, for example, to treat severe acne.

4 Although Vitamin A is vital to health and has many benefits, too much of it can cause health problems. A very high dose of vitamin A in the form of retinol can cause tiredness, joint pain, dry skin, headache, sickness, hair loss, drowsiness, liver and bone damage and sight problems. Vitamin A also accumulates in the liver and taking it over a long period of time can cause dry thickening of the skin, cracking of lips, damage to the eyes, skin reddening, hair loss, brittle bones, joint pain, lasting headache, increased pressure inside the skull and liver damage. Some, but not all, of these effects are reversible on reducing vitamin A intake.

5 Although it is broken down in the body to produce retinol, eating vegetables that are rich in beta-carotene, or consuming beta-carotene itself, does not result in adverse effects (except possibly high dose supplements in smokers) because less than one-third of beta-carotene from plant sources gets absorbed by the body.

6 Eating fat-rich food increases the absorption of vitamin A from the digestive system. The vitamin is carried on proteins in the blood to the liver, where it is stored and then distributed to the rest of the body to perform its functions. Vitamin A is excreted from the body largely in the urine, but as it builds up in the liver, more

comes out in the bile, which may prevent the liver from being exposed to too much of it.

Effects of vitamin A on reproduction

7 Vitamin A is necessary for the proper functioning of the male and female reproductive systems and both too little and too much can harm the unborn fetus. This paper is concerned with the effects of too much vitamin A (rather than too little) and ill-effects from over-exposure have been seen both in experimental animals and in humans. Too much vitamin A can cause malformations to the fetus that include spina bifida (abnormal development of the spine), small or no eyes, harelip, cleft palate, absent or deformed ears, and deformities of limbs, kidneys, genitals, heart, thyroid gland and skeleton.

8 The UK Government recommends that, in order to avoid possible harm to the unborn child, pregnant women, or women thinking about having a baby or trying to conceive, should not consume liver or liver products such as paté, or supplements that contain vitamin A, including fish liver oil, unless they are advised to do so by a doctor. The European Food Safety Authority (EFSA) set a Tolerable Upper Intake Level (UL) for vitamin A of 3,000 micrograms per day (3/1000 of a gram) for women of childbearing age, based on the risk of damage to the liver and to any unborn child. The UK Expert Committee on Vitamins and Minerals (EVM) considered that an intake greater that 1,500 micrograms per day was “inappropriate”, based on possible effects on bone. The World Health Organisation (WHO) recommends that vitamin A supplements should not be given to pregnant women except to prevent night blindness in places where vitamin A deficiency is a severe public health problem (which does not include the UK).

9 Taking food supplements, like fortified food products and vitamin pills, is the most common way for people, including pregnant women and those considering pregnancy, to be exposed to high doses of vitamin A. Scientific studies have surveyed the effects of supplements on development of the fetus in humans where women have taken higher dose supplements during pregnancy. Malformations have been seen, but as the number of women taking these supplements was low, the actual amount of vitamin A that causes deformities in humans remains uncertain.

10 Treatment of acne by taking tablets of the drug isotretinoin (“eye-soh-tret-in-oh-in”), a potent synthetic form of retinoic acid, is very effective but has raised concern as a possible cause of malformations when taken by pregnant women. Some countries, including Canada and the EU countries advise women against becoming pregnant while taking isotretinoin. But there are still a few women who become pregnant while taking this drug, putting the fetus at potential risk.

11 Treating acne with creams and ointments that contain forms of vitamin A and/or synthetic substances that mimic it, appears to pose a much lower level of risk to the unborn child than treatments given by mouth. However, since these preparations are also known to be able to produce the same adverse effects on the

fetus as tablets, when given at a sufficiently high dose, their use is likewise not recommended during pregnancy.

12 Concerns have been raised about a link between isotretinoin use and an increased risk of depression and suicide. However, recent evidence suggests that having acne can itself cause depression and hence, if anything, treatment with vitamin A analogues can improve mental health. Nevertheless, as explained above, women who are pregnant or trying to conceive should avoid taking isotretinoin because of the possible risk to the fetus.

13 The effects of vitamin A may be affected by

a. other components in the diet, including vitamins D, K, C and folate, some fats and zinc,
b. alcohol,
c. medicines including antibiotics, treatments for fungal infections, drugs for epilepsy, and
d. chemicals in the environment including biocidal ship antifouling paints (i.e. paints that discourage growth of marine organisms) and flame retardants, for example from furniture.

One way they can do this is by affecting the rate of breakdown of vitamin A and its active products.

14 Consuming large amounts of beta-carotene, for example by eating a lot of carrots daily, may lead to some skin yellowing and a fall in the levels of vitamin A in the liver but, unlike intake of pre-formed vitamin A, studies on animals have shown no ill-effects of beta-carotene on their offspring.

15 A study showed that high intake of beta-carotene supplements, as part of a clinical trial, unexpectedly increased the incidence of lung cancer and overall mortality in smokers. However, smoking itself can damage the fetus, regardless of any additional adverse effects caused by consumption of beta-carotene, so women are anyway strongly advised against smoking during pregnancy.

16 In many regions of the world, including part of Africa and south-west Asia, there is more concern about vitamin A deficiency and the harmful effects this has upon the health of unborn children. In developed countries (like the UK, USA and those in Europe), however, the concern is more about excess intake, as many people regularly consume more than the recommended daily amount, and in some cases, more than EFSA's tolerable upper limit.

17 EFSA has estimated that most European adults consume between 816 and 1,498 micrograms of retinol per day. The UK Government dietary advice, on the NHS.uk website recommends a daily vitamin A intake from food, for those aged 19 to 64, of 700 micrograms for men and 600 micrograms for women.. Official estimates are that in the UK women between 16 and 49 years of age actually have an intake of between 760 and 2600 micrograms per day, and the small number who regularly eat

liver and liver products such as paté may consume up to 3 times this amount. Supplements containing vitamin A in the form of retinol can add 300 – 906 micrograms per serving. Pregnant women and women thinking about having a baby are therefore specifically warned to avoid taking supplements containing vitamin A and not to eat liver and liver products to avoid potential harm to the unborn child, unless specifically advised to do so by their Doctor. No other food provides as much vitamin A on its own, although some fortified spreads and "health foods" may, in combination, provide more than the recommended limit.

18 Food supplements containing beta-carotene do not have warnings against their use by pregnant women and women thinking about having a baby because this nutrient is considered low risk.

19 Since there is still a lot of uncertainty about how much vitamin A is likely to cause deformities in unborn children, the COT agree that the current UK Government advice to pregnant women and those planning pregnancy – as set out on NHS.uk website - that they should limit their intake of vitamin A to reduce this risk, remains appropriate.