1 **DRAFT SCIENTIFIC OPINION**

2 Scientific Opinion on Dietary Reference Values for phosphorus[1]

3 **EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)**[2,3]

4 European Food Safety Authority (EFSA), Parma, Italy

5 **ABSTRACT**

6 Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies
7 (NDA) derived Dietary Reference Values (DRVs) for phosphorus. The Panel considered evidence from balance
8 studies and studies on phosphorus intake and long-term health outcomes and concluded that there are no new
9 data to amend the basis used by the SCF (1993) for setting the previous Population Reference Intakes (PRIs) for
10 phosphorus, which were derived from the equimolar relationship between calcium and phosphorus. The Panel
11 thus considered setting DRVs for phosphorus in line with those for calcium. This criterion for setting DRVs for
12 phosphorus is based on the lack of consistent other evidence and takes into consideration that phosphorus and
13 calcium are present in the body in approximately equimolar amounts. The Panel noted that the fractional
14 absorption of phosphorus is higher compared to calcium. As absorption of both minerals may vary with age and
15 other dietary components, the Panel considered that the exact calcium-to-available phosphorus ratio cannot be
16 determined and proposed to set DRVs for phosphorus based on the equimolar calcium-to-phosphorus ratio.
17 Adequate Intakes (AIs) are proposed for all population groups and are 200 mg/day for infants aged 7–11 months,
18 between 300 and 800 mg/day for children and 700 mg/day for adults. Taking into consideration adaptive changes
19 in phosphorus metabolism that occur during pregnancy and lactation, the AI for adults also applies to pregnant
20 and lactating women.

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23 **KEY WORDS**

24 phosphorus, calcium, Adequate Intake, Dietary Reference Value

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SUMMARY

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on Dietary Reference Values for the European population, including phosphorus.

Phosphorus is involved in many physiological processes, such as the cell's energy cycle, regulation of the body's acid–base balance, as a component of the cell structure, in cell regulation and signalling, and in the mineralisation of bones and teeth. About 85 % of the body's phosphorus is in bone and teeth, 14 % in soft tissues, including muscle, liver, heart and kidneys, and only 1 % is present in extracellular fluids. Phosphorus homeostasis is intricately linked to that of calcium because of the actions of calcium-regulating hormones, such as parathyroid hormone (PTH) and 1,25-dihydroxy-vitamin D ($1,25(OH)_2D_3$), at the level of the bone, the gut, and the kidneys.

Phosphorus absorption occurs through passive diffusion and sodium-dependent active transport and via paracellular and cellular pathways. In adults, net phosphorus absorption typically ranges from 55–80 % of intake. Phosphorus absorption is affected by the total amount of phosphorus in the diet and also by the type (organic versus inorganic), food origin (animal- versus plant-derived), and ratio of phosphorus to other dietary components. Absorption is regulated by $1,25(OH)_2D_3$ and PTH.

Hypophosphataemia, defined by a serum inorganic phosphorus concentration < 0.80 mmol/L (2.48 mg/dL), only rarely occurs because of inadequate dietary phosphorus intake, and is almost always due to metabolic disorders.

The major dietary contributors to phosphorus intake are foods high in protein content, i.e. milk and milk products followed by meat, poultry and fish, grain products and legumes. Based on data from up to nine EU countries, mean phosphorus intakes range between 265 and 531 mg/day in infants, between 641 and 973 mg/day in children aged 1 to < 3 years, between 750 and 1 202 mg/day in children aged 3 to < 10 years, between 990 and 1 601 mg/day in children aged 10 to < 18 years, and between 1 000 and 1 767 mg/day in adults (≥ 18 years).

Balance studies in adults were considered to be heterogeneous and to have many limitations. Overall, balance studies, including those in children and pregnant women, could not be used for setting DRVs for phosphorus.

Evidence from human studies on the relationship between phosphorus intake and various health outcomes was also reviewed. It was considered that data on measures of bone health, cancer-related outcomes and evidence related to all-cause mortality and cardiovascular outcomes could not be used to derive DRVs for phosphorus.

It was concluded that there are no new data to amend the the basis used by the SCF (1993) for setting the previous Population Reference Intakes (PRIs) for phosphorus, which were derived from the equimolar relationship between calcium and phosphorus. It was thus considered to set DRVs for phosphorus in line with those for calcium. This criterion for setting DRVs for phosphorus is based on the lack of consistent other evidence and takes into consideration that phosphorus and calcium are present in the body in approximately equimolar amounts. It was noted that the fractional absorption of phosphorus is higher compared to calcium. As absorption of both minerals may vary with age and other dietary components, it was considered that the exact calcium-to-available phosphorus ratio cannot be determined, and DRVs for phosphorus were proposed to be again based on the equimolar calcium-to-phosphorus ratio. As the available data are insufficient to derive ARs and PRIs for phosphorus, it was proposed to set AIs for all population groups. AIs are 200 mg/day for infants aged 7–11 months, between 300 and 800 mg/day for children and 700 mg/day for adults. Taking into consideration adaptive changes in phosphorus metabolism that occur during pregnancy and lactation, it was considered that the AI for adults also applies to pregnant and lactating women.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The scientific advice on nutrient intakes is important as the basis of Community action in the field of nutrition, for example such advice has in the past been used as the basis of nutrition labelling. The Scientific Committee for Food (SCF) report on nutrient and energy intakes for the European Community dates from 1993. There is a need to review and, if necessary, to update these earlier recommendations to ensure that the Community action in the area of nutrition is underpinned by the latest scientific advice.

In 1993, the SCF adopted an opinion on the nutrient and energy intakes for the European Community.[4] The report provided Reference Intakes for energy, certain macronutrients and micronutrients, but it did not include certain substances of physiological importance, for example dietary fibre.

Since then new scientific data have become available for some of the nutrients, and scientific advisory bodies in many European Union Member States and in the United States have reported on recommended dietary intakes. For a number of nutrients these newly established (national) recommendations differ from the reference intakes in the SCF (1993) report. Although there is considerable consensus between these newly derived (national) recommendations, differing opinions remain on some of the recommendations. Therefore, there is a need to review the existing EU Reference Intakes in the light of new scientific evidence, and taking into account the more recently reported national recommendations. There is also a need to include dietary components that were not covered in the SCF opinion of 1993, such as dietary fibre, and to consider whether it might be appropriate to establish reference intakes for other (essential) substances with a physiological effect.

In this context EFSA is requested to consider the existing Population Reference Intakes for energy, micro- and macronutrients and certain other dietary components, to review and complete the SCF recommendations, in the light of new evidence, and in addition advise on a Population Reference Intake for dietary fibre.

For communication of nutrition and healthy eating messages to the public it is generally more appropriate to express recommendations for the intake of individual nutrients or substances in food-based terms. In this context the EFSA is asked to provide assistance on the translation of nutrient based recommendations for a healthy diet into food based recommendations intended for the population as a whole.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1)(a) and Article 31 of Regulation (EC) No. 178/2002,[5] the Commission requests EFSA to review the existing advice of the Scientific Committee for Food on population reference intakes for energy, nutrients and other substances with a nutritional or physiological effect in the context of a balanced diet which, when part of an overall healthy lifestyle, contribute to good health through optimal nutrition.

In the first instance EFSA is asked to provide advice on energy, macronutrients and dietary fibre. Specifically advice is requested on the following dietary components:

- Carbohydrates, including sugars;

[4] Scientific Committee for Food, Nutrient and energy intakes for the European Community, Reports of the Scientific Committee for Food 31st series, Office for Official Publication of the European Communities, Luxembourg, 1993.

[5] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1-24.

- Fats, including saturated fatty acids, polyunsaturated fatty acids and monounsaturated fatty acids, *trans* fatty acids;
- Protein;
- Dietary fibre.

Following on from the first part of the task, EFSA is asked to advise on population reference intakes of micronutrients in the diet and, if considered appropriate, other essential substances with a nutritional or physiological effect in the context of a balanced diet which, when part of an overall healthy lifestyle, contribute to good health through optimal nutrition.

Finally, the EFSA is asked to provide guidance on the translation of nutrient based dietary advice into guidance, intended for the European population as a whole, on the contribution of different foods or categories of foods to an overall diet that would help to maintain good health through optimal nutrition (food-based dietary guidelines).

ASSESSMENT

1. Introduction

Phosphorus is an essential nutrient and is involved in many physiological processes, such as the cell's energy cycle, regulation of the body's acid–base balance, as a component of the cell structure, in cell regulation and signalling, and in the mineralisation of bones and teeth.

In 1993, the Scientific Committee for Food (SCF, 1993) adopted an opinion on nutrient and energy intakes for the European Community and derived for phosphorus a Lowest Threshold Intake, an Average Requirement (AR) and a Population Reference Intake (PRI) for adults. The SCF also set PRIs for infants from six months, for children and for pregnancy and lactation.

2. Definition/category

In the human body, phosphorus is present in different forms. Serum contains mainly inorganic phosphates (dihydrogen and monohydrogen phosphate), bone contains phosphorus largely in the form of hydroxyapatite, while the soft tissues and extracellular fluids contain organic phosphates in complex with carbohydrates, lipids and proteins (Bansal, 1990). In this opinion, the term phosphorus is used for consistency and simplicity when referring to its presence in blood or bone.

2.1. Chemistry

Phosphorus is the 11th most common element in the earth's crust. It is a non-metal, solid chemical element, found in the nitrogen group, i.e Group 15 (VA) of the periodic table. It has the atomic number 15 and an atomic mass of 31 Da. Phosphorus has several oxidation states, the most important being +3 and +5 (RSC, 2004; Kalantar-Zadeh et al., 2010; Corbridge, 2013). Phosphorus does not occur in nature as a free element due to its high reactivity but is found in the form of phosphate minerals. The most abundant form is apatite (and related minerals), hydroxyapatite [$Ca_{10}(OH)_2(PO_4)_6$], chlorapatite [$Ca_{10}Cl_2(PO_4)_6$] and fluorapatite [$Ca_{10}F_2(PO_4)_6$]. There is only one stable phosphorus isotope, i.e. ^{31}P. There are, however, at least six known radioactive isotopes with highly variable, usually very short, half-lives ranging from a few nanoseconds to a few seconds. Only two radioactive isotopes (^{32}P and ^{33}P) exist long enough to be measured. ^{32}P has a half-life of 14 days and has applications in medicine, industry and in tracer studies. ^{33}P has a half-life of 25 days and it also has tracer applications (Audi et al., 2003).

2.2. Function of phosphorus

2.2.1. Biochemical functions

Phosphorus is the main mineral constituent of bones and one of the most abundant minerals in the body. About 85 % of the body's phosphorus is in bone and teeth, in the form of hydroxyapatite, and together these two minerals account for around 80–90 % of bone composition. Hydroxyapatite forms the mineralized matrix of bone and contributes to the unique biomechanical properties of bone. Phosphorus homeostasis is intricately linked to that of calcium because of the actions of calcium-regulating hormones, such as parathyroid hormone (PTH) and 1,25-dihydroxy-vitamin D ($1,25(OH)_2D_3$), at the level of the bone, the gut, and the kidneys.

The remaining 15 % of phosphorus present in the body is integral to diverse functions ranging from the transfer of genetic information to energy utilisation. Phosphorus is a structural component of the nucleic acids DNA and RNA and thus is involved in the storage and transmission of genetic material. It is an essential component of phospholipids (e.g., phosphatidylcholine) that form all membrane bilayers throughout the body. They are essential for optimal brain health and influence brain cell communication processes and receptor functions. Many proteins, enzymes, and sugars in the body are phosphorylated, and that process often dictates the activity and function of phosphoproteins and sugars. Phosphorus is an integral component of the body's key energy source, adenosine triphosphate (ATP). Other phosphorylated molecules (e.g., creatine phosphate in muscle) serve as a rapid source of

phosphate for ATP production. Phosphorus, as 2,3-diphosphoglycerate (also known as 2,3-bisphosphoglycerate), plays a vital role in the dissociation of oxygen from haemoglobin. Cellular phosphate is the main intracellular buffer and therefore is essential for pH regulation of the human body. Finally, many intracellular signalling processes depend on phosphorus-containing compounds such as cyclic adenosine monophosphate (cAMP), cyclic guanine monophosphate (cGMP) and inositol polyphosphates (e.g., inositol triphosphate or IP3) (O´Brien et al., 2014).

2.2.2. Health consequences of deficiency and excess

2.2.2.1. Deficiency

Phosphorus deficiency presents as hypophosphataemia, i.e. serum phosphorus concentration is below 0.80 mmol/L (2.48 mg/dL). This only rarely occurs because of inadequate dietary phosphorus intake, and is almost always due to metabolic disorders. Although rare in the general population, the incidence of hypophosphataemia is high in certain subgroups of patients, such as those with sepsis, chronic alcoholism, major trauma, or chronic obstructive pulmonary disease (Gaasbeek and Meinders, 2005; Brunelli and Goldfarb, 2007). Hyphosphataemia may also occur during diabetic ketoacidosis because the administration of insulin drives glucose and phosphorus into cells and causes a rapid fall in serum phosphorus concentration. Mild hypophosphataemia can also occur as a common generally asymptomatic consequence of hyperparathyroidism (O´Brien et al., 2014).

The clinical symptoms due to hypophosphataemia usually occur when serum phosphorus concentrations fall below 0.3 mmol/L (~1 mg/dL), particularly when this is associated with total body phosphorus depletion. The nature and severity of the clinical symptoms depend on the extent of the phosphorus depletion and are highly variable according to the underlying cause and the individual patient's status (Brunelli and Goldfarb, 2007). At a whole organism level, the effects of hypophosphataemia include anorexia, anaemia, muscle weakness, bone pain, rickets and osteomalacia, increased susceptibility to infection, paresthesia, ataxia, confusion, and even death. The muscle weakness involves especially proximal muscle groups, and when prolonged or severe can lead to muscle fibre degeneration. The skeleton will exhibit either rickets or osteomalacia, depending on growth status. In both, the disorder consists of a failure to mineralise forming growth plate cartilage or bone matrix, together with impairment of chondroblast and osteoblast function. This functional disturbance both slows osteoid deposition and disturbs the normal maturation process in the hypertrophic zone of the growth cartilage (Heaney, 2012).

2.2.2.2. Excess

In 2005, EFSA (2005) concluded that the available data were not sufficient to establish a Tolerable Upper Intake Level (UL) for phosphorus. Adverse effects of excessive phosphorus intake, such as hyperphosphataemia, leading to secondary hyperparathyroidism, skeletal deformations, bone loss, and/or ectopic calcification have been reported in animal studies. However, such effects were not observed in studies in humans, except in patients with end stage renal disease. Although an increase in serum PTH concentration was found in acute or short-term loading studies, no significant changes could be demonstrated in longer term studies with dosages up to 3 000 mg/day. In these studies, no evidence was found for effects on markers of bone remodelling. Similarly, no convincing evidence was found to support suggestions that high phosphorus diets would aggravate the effects of a state of secondary hyperparathyroidism induced by inadequate calcium intake, or an inadequate vitamin D status.

Gastrointestinal symptoms, such as osmotic diarrhoea, nausea and vomiting, were observed in some healthy subjects taking phosphorus (phosphate) supplements with dosages higher than 750 mg/day, but these symptoms were not considered to be a suitable basis for establishing a UL for phosphorus from all sources (EFSA, 2005).

2.3. Physiology and metabolism

2.3.1. Intestinal absorption

Phosphorus is absorbed with high efficiency. In adults, for example, net phosphorus absorption typically ranges from 55 to 80 % of intake, and in infants from 65 to 90 % (Heaney, 2012; O´Brien et al., 2014). Intestinal phosphorus absorption tends to decrease with ageing. Dietary phosphorus reaches the absorptive surfaces of the enterocyte in the form of inorganic phosphorus or organic phosphorus complexes. Within the gut lumen, phosphatases help to digest and hydrolyse the organic forms into inorganic phosphorus. Inorganic phosphorus is absorbed along the entire intestine, with the small intestine having a significantly higher absorption capacity compared to the colon (Sabbagh et al., 2011). Dietary phosphorus, $1,25(OH)_2D_3$, and PTH are thought to be the most important physiological regulators of intestinal phosphorus absorption, although epidermal growth factor, glucocorticoids, oestrogens, metabolic acidosis, phosphatonins and secreted frizzled related protein-4 also affect intestinal phosphorus absorption (Penido and Alon, 2012).

There are two pathways for intestinal absorption of inorganic phosphorus, i.e. paracellular and cellular (Sabbagh et al., 2011; Penido and Alon, 2012), and at least two mechanisms, i.e. passive diffusion (McHardy and Parsons, 1956) and sodium-dependent active transport (Walton and Gray, 1979; Eto et al., 2006). Most phosphorus absorption occurs in the small intestine by load-dependent passive absorption. Paracellular absorption occurs at tight junctions and utilises electrochemical gradients. These are thought to be regulated by signal transduction pathways but the specific mechanism for phosphate has not yet been identified (Sabbagh et al., 2011). Cellular absorption requires sodium-dependent phosphate transporters which include NaPi-IIa (SLC34A1), NaPi-IIb (SLC34A2 or NPT2b) and NaPi-IIc (SLC34A3) and are also expressed in the renal tubule, but it is NaPi-IIb which is predominant in the intestine (Penido and Alon, 2012; Biber et al., 2013). The relative proportion of absorption via each mechanism varies depending on the luminal phosphate concentration, with active transport contributing between 30 and 80 % (Sabbagh et al., 2011).

The sodium-dependent phosphate transporter NaPi-IIb can be modulated by low dietary inorganic phosphorus, several hormones and vitamin D (Segawa et al., 2004; Forster et al., 2011; Sabbagh et al., 2011) and the mucosa of the duodenum is particularly responsive to low inorganic phosphorus intake (Marks et al., 2010). Administration of $1,25(OH)_2D_3$ to vitamin D-deficient animals resulted in up-regulation of transporters and significantly increased inorganic phosphate absorption (Katai et al., 1999; Kido et al., 2013). Despite some evidence of an impact of vitamin D on phosphorus absorption in humans (Brickman et al., 1977), the net result is probably small and the actual effect of vitamin D on adult phosphorus absorption under usual conditions and in health remains unclear (Heaney, 2012). The small intestine and kidneys work together to maintain circulating levels of inorganic phosphorus (Marks et al., 2010; Biber et al., 2013), although the exact mechanism of how phosphorus is “sensed” has not yet been identified (Bergwitz and Jüppner, 2011). In view of earlier studies identifying the continuation of intestinal phosphorus absorption even in the presence of high blood concentrations of phosphorus (Brickman et al., 1974; IOM, 1997), it is unclear whether this regulation may be overwhelmed by high dietary intake.

The ability to absorb and use phosphorus is affected by the total amount of phosphorus in the diet and also by the type (organic versus inorganic), food origin (animal- versus plant-derived), and ratio of phosphorus to other dietary components. Most food phosphorus is in the form of readily hydrolysable organic phosphate esters, with the exception of seed foods and unleavened breads. In fact, phytic acid (the storage form of phosphorus in plants) cannot be digested because humans lack the enzyme phytase. Colonic bacteria, which do possess phytase, are able to release some of that phosphorus for absorption. Additionally, yeasts can hydrolyse phytic acid, and hence leavened cereal-grain foods (e.g. many breads) exhibit good phosphorus bioavailability (Heaney, 2012). Apart from phytate, the principal factor influencing phosphorus bioavailability is not the food itself, but co-ingested calcium, which binds phosphorus in the digestate and prevents its absorption. Phosphorus originating from food

additives, i.e. already in an ionised inorganic form, is absorbed more readily (Kalantar-Zadeh et al., 2010).

2.3.2. Transport in blood

Phosphorus is present in the blood in both organic and inorganic forms. Approximately 70 % of phosphorus in the blood is in the form of organic compounds, including phospholipids, i.e. in blood cell membranes and plasma lipoproteins. Of the remaining 30 %, most (~85 %) is present as inorganic phosphorus, while a small percentage is found complexed with sodium, calcium and magnesium as salts in the blood.

In plasma, phosphate ions HPO_4^{2-} and $H_2PO_4^-$ exist in a pH-dependent equilibrium. About 85–90 % of serum phosphate is free and is ultrafiltrable; 10–15 % is bound to protein. The normal mean concentration of phosphate in human plasma is 0.8–1.5 mmol/L, which is maintained within this physiological range by regulation of dietary absorption, bone formation, and renal excretion, as well as equilibration with intracellular stores. Plasma phosphorus fluctuates with age (it is higher in children than adults), dietary intake, and acid–base status. Serum phosphorus concentration increases somewhat in response to ingestion of phosphorus (Marks et al., 2010) (see Section 2.4.1.1). The increased serum phosphorus concentration then depresses the serum calcium ion concentration, which in turn stimulates the parathyroid glands to synthesise and secrete PTH. PTH acts on bone and the kidneys to correct the modest decline in Ca^{2+} and homeostatically return it to the set level. It has been suggested that an elevation of serum phosphorus ionic concentration directly influences PTH secretion independently of hypocalcaemia (O´Brien et al., 2014). These meal-associated fluctuations in phosphorus and Ca^{2+} are part of normal physiological adjustments that occur typically three or more times a day. The blood concentration of phosphorus is less tightly regulated than the serum calcium concentration. Wider fluctuations in serum phosphorus concentration reflect both dietary intake and cellular release of inorganic phosphates (Anderson, 2005). There is diurnal variation (Jubiz et al., 1972; Moe et al., 2011), with values being lowest in the morning and rising during the day (Pocock et al., 1989).

2.3.3. Distribution to tissues

Phosphorus, as phosphate, is the most abundant anion in the human body and comprises approximately 1 % of total body weight (Farrow and White, 2010; Penido and Alon, 2012). Approximately 85 % of phosphorus is present in bone and teeth, with the remainder distributed between other tissues (14 %) and extracellular fluid (1 %) (O´Brien et al., 2014). Thus, similar to calcium, serum measurements only reflect a minor fraction of total body phosphorus, and therefore do not consistently reflect total body stores (Moe, 2008). Intracellular phosphorus exists in the form of organic compounds such as ATP and as free phosphate anions (e.g. PO_4^{3-}) (Takeda et al., 2012). Cells hold very limited reserves of inorganic phosphorus relying on supply by extracellular fluid (IOM, 1997). In bone, phosphorus is primarily complexed with calcium in the form of hydroxyapatite crystals; the remaining phosphate appears as amorphous calcium phosphate (Farrow and White, 2010). In soft tissue and cell membranes, phosphorus exists mainly as phosphate esters and to a lesser extent as phosphoproteins and free phosphate ions. In the extracellular fluid, about one-tenth of the phosphorus content is bound to proteins, one-third is complexed to sodium, calcium, and magnesium, and the remainder is present as inorganic phosporus (Penido and Alon, 2012).

In pregnancy, especially in the third trimester, inorganic phosphorus moves from the mother to the fetus against a concentration gradient (Brunette et al., 1986; Husain and Mughal, 1992). This is a sodium-dependent, energy-requiring process facilitated by NaPi-IIb (SLC34A2) transporters, which are expressed in the placental labyrinthine cells (Mitchell and Jüppner, 2010). The placenta meets the fetal need by actively transporting phosphorus from the maternal circulation. Phosphorus is maintained in the fetal circulation at higher concentrations than in the mother, and such high levels appear necessary for the developing skeleton to accrete a normal amount of phosphorus by term. However, the factors and the molecular mechanism controlling placental phosphorus transport have not yet been explored (Mitchell and Jüppner, 2010; Kovacs, 2014). Phosphorus rises over the first 24–

48 hours after delivery; after that, it declines toward adult values, consistent with resolution of transient hypoparathyroidism in the newborn (Kovacs, 2014).

2.3.4. Storage

Total body phosphorus in adults is typically in the order of 400–800 g, and most of this is located in the bones and teeth (Moe, 2008).

At birth, a neonate contains roughly 20 g phosphorus (0.5 g/100 g fat free tissue), most of which is accumulated during the last eight weeks of pregnancy (Widdowson and Spray, 1951). Assuming continuous growth and maturity at 18 years it has been estimated that phosphorus accretion rates are 107 mg/day in boys and 80 mg/day in girls, with a peak rate in adolescence of 214 mg/day (Prentice and Bates, 1994).

2.3.5. Metabolism

In adults, a regular Western diet provides on average about 20 mg phosphorus/kg body weight per day (Calvo et al., 2014). Of this, approximately 16 mg/kg per day is absorbed in the proximal intestine, predominantly in the jejunum. Approximately 3 mg/kg per day is secreted into the intestine via pancreatic, biliary, and intestinal secretions, giving a net phosphorus absorption of approximately 13 mg/kg per day, while 7 mg/kg per day appear in the faeces. The absorbed phosphorus enters the extracellular fluid pool and moves in and out of bone as needed (around 3 mg/kg per day) (Penido and Alon, 2012).

The absorbed phosphorus enters the exchangeable phosphorus pool which consists of the intracellular phosphorus (70 %), the phosphorus arising from bone remodelling (29 %) and the phosphorus in serum (< 1 %). Exit from the exchangeable pool is through skeletal deposition, renal excretion, and intestinal secretion. Under physiological conditions in adults, the amount of phosphorus entering the phosphorus pool from bone resorption equals that exiting the pool for bone formation (Hruska et al., 2008). Both the intestine and the kidneys are involved in phosphate homeostasis by serving as regulators of phosphorus absorption from the diet (in the inorganic form) and phosphorus excretion (in the inorganic form), respectively (Berndt and Kumar, 2007).

Phosphorus homeostasis is tightly regulated by the bone–kidney–parathyroid gland axis. The key hormones contributing to the regulation of phosphorus homeostasis are PTH, the active metabolite of vitamin D, i.e. $1,25(OH)_2D_3$ (calcitriol), and the phosphatonin fibroblast growth factor-23 (FGF-23), mainly produced and secreted by osteocytes in bone (Berndt and Kumar, 2009; Bergwitz and Juppner, 2010). An elevation in serum phosphorus following a diet high in phosphorus leads to a decrease in serum calcium concentration and an increase in PTH release resulting in an increased renal phosphate excretion. The increase in serum inorganic phosphate additionally results in a reduced $1,25(OH)_2D_3$ synthesis which in turn leads to a reduced intestinal phosphorus absorption (Berndt and Kumar, 2009; Bergwitz and Juppner, 2010). An increase in serum phosphorus also results in an increased secretion of FGF-23 by the osteocytes which directly stimulates the renal fractional excretion of phosphorus and induces a reduction in the $1,25(OH)_2D_3$ concentration, with a subsequent decrease in intestinal phosphorus absorption (Quarles, 2008). On the other hand, a decrease in serum phosphorus following a diet low in phosphorus results in an increase in serum calcium concentrations and a decrease in PTH release resulting in a decreased renal phosphorus excretion. Additionally, a decrease in serum phosphorus leads to an increased $1,25(OH)_2D_3$ synthesis and subsequent enhanced phosphorus absorption by the intestine (Berndt and Kumar, 2009; Bergwitz and Juppner, 2010). Finally, a decrease in serum phosphorus reduces serum FGF-23, thus restoring the concentration of serum phosphorus (Quarles, 2008).

2.3.6. Elimination

2.3.6.1. Urine

The kidney plays a predominant role in the regulation of systemic phosphorus homeostasis. About 80 % of filtered phosphorus is reabsorbed in the proximal tubule. There is likely no reabsorption of phosphorus in the loop of Henle and the collecting duct. Some evidence has been provided that in distal nephron segments approximately 5 % of filtered phosphorus may be reabsorbed. Under normal conditions, about 15 % of the filtered phosphorus is ultimately excreted (Bindels et al., 2012). When an individual is in phosphorus equilibrium (i.e. not gaining or losing phosphorus), the amount of phosphorus excreted in the urine (1–1.5 g/24 hours) is equivalent to the amount of phosphorus absorbed in the intestine (Berndt and Kumar, 2007). The tubular reabsorption of phosphorus is saturable, that is, when the serum phosphorus concentration exceeds the renal threshold, phosphorus begins to appear in the urine, increasing in proportion to the filtered load (Bindels et al., 2012).

The reabsorption of inorganic phosphorus in the kidney occurs along with sodium via specific sodium phosphate co-transporters (Tenenhouse and Murer, 2003). The main transporter involved in this process is NaPi-IIa (Tenenhouse, 2005). Controlling the number of this transporter leads to regulation of phosphorus reabsorption in the kidney. Factors that increase tubular phosphorus reabsorption include low intake of phosphorus and high intake of potassium, parathyroidectomy, $1,25(OH)_2D_3$, hypocalcaemia, volume contraction and hypocapnia (i.e. a state of reduced carbon dioxide in the blood), whereas factors that decrease phosphorus tubular reabsorption include a diet high in phosphorus and low in potassium, PTH, volume expansion, hypercalcaemia, carbonic anhydrase inhibitors, glucose and alanine, acid–base disturbances, increased bicarbonate, hypercapnia, metabolic inhibitors, FGF-23 and frizzled receptor protein 4 (Schiavi and Kumar, 2004; Berndt and Kumar, 2009). Phosphatonins, and in particular FGF-23, are also postulated to be involved in phosphorus homeostasis in pathophysiological conditions associated with phosphorus wasting. Nevertheless, it remains unclear whether and how phosphatonins are involved in normal phosphorus homeostasis (Berndt and Kumar, 2009).

Clearance studies have demonstrated that phosphorus excretion is remarkably responsive to antecedent dietary phosphorus intake. The phosphorus reabsorption capacity adapts to altered intake of phosphorus within hours (acute adaptation) and remains changed during prolonged intake of altered amounts of dietary phosphorus. Fractional excretion of phosphorus increases with a high phosphorus diet and decreases with a low phosphorus diet (Bindels et al., 2012).

2.3.6.2. Faeces

Faecal excretion of phosphorus has been reported to range from about 300–600 mg/day (Greger et al., 1978; Anderson, 2005; Delgado-Andrade et al., 2011). Total faecal phosphorus, however, represents partly non-absorbed phosphorus from food, and partly endogenous phosphorus. The endogenous fraction of faecal phosphorus is mainly derived from non-reabsorbed digestive secretions (approximately 3 mg phosphorus/kg body weight per day as a component of digestive pancreatic and intestinal enzymes) and from desquamated epithelia of the gut (Kjerulf-Jensen, 1941). Endogenous faecal phosphorus excretion is responsive to alterations in dietary phosphorus intake and ranges between 0.9 and 4 mg/kg body weight per day (O´Brien et al., 2014).

2.3.6.3. Sweat

Sweat is not an important source of phosphorus elimination. Very small quantities of phosphorus in sweat (0.45–0.81 mg/hour) have been reported following a phosphorus-rich meal challenge (Consolazio et al., 1963).

2.3.6.4. Breast milk

The phosphorus concentration of human milk increases during early lactation and then gradually declines with progressing lactation. From 30 days of lactation, Atkinson et al. (1995) reported an average phosphorus concentration in human milk of about 140 mg/L (4.5 mmol/L).

Following a comprehensive literature search for studies published from the year 2000 onwards, five studies were retrieved which reported on the phosphorus concentration of breast milk. Three studies reported phosphorus concentrations of mature milk from women in Europe, whereas the other two studies covered women living in Australia and Mexico and did not report on the stage of lactation. Phosphorus concentrations were (mean ± SD) 172 ± 23 mg/L in 60 women in Sweden at 14–21 days of lactation (Bjorklund et al., 2012), (median (range)) 123.7 (76.9–159.7) mg/L in 10 Caucasian women in the UK at 9–13 weeks of lactation (Nickkho-Amiry et al., 2008), and 130 mg/kg of breast milk (mean) in nine milk samples from Polish women at 5–6 months of lactation (Witczak and Jarnuszewska, 2011).

Gidrewicz and Fenton (2014) published a systematic review and meta-analysis of 41 studies of breast milk composition. Data on phosphorus concentration of breast milk from mothers of term infants were available from seven studies, and these results are summarised in the table below.

Table 1: Breast milk phosphorus concentration (mg/L) over time in studies with mothers of term infants according to Gidrewicz and Fenton (2014)

Time post partum	Breast milk phosphorus concentration (mg/L)		
	Mean	SD	n
Day 1–3	110	30	6
Day 4–7	130	40	86
Week 2	150	40	90
Week 3–4	160	30	75
Week 5–6	160	30	213
Week 7–9	160	30	363
Week 10–12	140	30	13

SD, standard deviation; n, number of samples
Based on data reported in seven studies also having a group of mothers of term infants (Atkinson et al., 1980; Gross et al., 1980; Sann et al., 1981; Lemons et al., 1982; Butte et al., 1984b; Mataloun and Leone, 2000; Yamawaki et al., 2005)

The Panel notes that no quantitative assessment of phosphorus resorption from bone during lactation is available. However, extended lactation is associated with a modest reduction in bone mineral density (BMD), with a return to baseline at 12 months after parturition (Sowers et al., 1993; Karlsson et al., 2001), independently of the length of lactation (Moller et al., 2012). The role of dietary phosphorus during pregnancy and lactation has not been established.

Prentice (2003) reviewed the evidence about biological adaptation mechanisms (increases in food intake, elevated gastro-intestinal absorption, decreased mineral excretion and mobilisation of tissue stores) required to preserve the maternal mineral economy while meeting the additional mineral requirements during pregnancy and lactation. The author concluded that both pregnancy and lactation are associated with physiological adaptive changes in mineral metabolism that are independent of maternal mineral supply within the range of normal dietary intakes. These adaptive processes provide the minerals necessary for fetal growth and breast milk production without requiring an increase in maternal dietary intake or compromising maternal bone health in the long term.

The Panel considers that around 140 mg/L (4.5 mmol/L) of phosphorus is secreted with mature human milk. The Panel acknowledges the existence of physiological adaptive processes that ensure sufficient phosphorus for fetal growth and breast milk production. These may obviate the need in pregnancy and lactation for additional phosphorus in the diet, provided intake is close to the DRV for adults.

2.3.7. Interaction with other nutrients

Calcium and phosphorus are present in the body in approximately equimolar amounts (Haynes et al., 2014) and are both required for bone mineral deposition and maintenance throughout life. Outside the skeleton, their essential but distinct physiological functions are controlled by specific transporters and hormonal systems, which also serve to secure the appropriate supply for bone health. Several interactions between phosphorus and calcium have been documented at both the intestinal and renal levels. Phosphate decreases urinary calcium excretion, and increases calcium balance (Fenton et al., 2009). A high phosphorus/low calcium diet and, inversely, a high calcium/low phosphorus diet can result in reduced absorption of the lower dose mineral which can lead to disturbances in calcium or phosphorus homeostasis, with possible detrimental consequences on bone health (EFSA NDA Panel, 2015).

2.4. Biomarkers

2.4.1. Biomarkers of intake

A precise assessment of dietary phosphorus intake in free-living individuals is difficult due to the questionable accuracy of dietary instruments used to estimate phosphorus in foods in all its forms, particularly inorganic sources from phosphorus-based food additives and dietary supplements (Calvo and Uribarri, 2013). Thus, there is a need for surrogate markers of phosphorus intake beyond dietary estimates.

2.4.1.1. Serum phosphorus concentration

Serum inorganic phosphorus has been proposed as an indicator of adequacy of phosphorus intake (IOM, 1997), mainly based on the equation proposed by Nordin B.E.C. (1989), derived from data from an infusion study (Bijovet, 1969). This equation has been established in adults with normal renal function and with amounts of infused phosphorus < 20 mmol/day (< 619 mg/day), while it became weaker at higher amounts of infused phosphorus. Since serum phosphorus concentrations are maintained within a relatively narrow range by different homeostatic mechanisms (Section 2.3.5), the effect of dietary phosphorus intake on serum phosphorus concentrations appears to be relatively small, even in the presence of wide variations in dietary phosphorus intake. The association between dietary phosphorus intake and serum phosphorus has been evaluated in 15 513 participants of the Third National Health and Nutrition Examination Survey (NHANES) in the USA (de Boer et al., 2009). Phosphorus intake was assessed by 24-hour dietary recall and 1-month food frequency questionnaire (FFQ). A weak but significant association of dietary phosphorus intake with serum phosphorus concentration was observed, with each 500 mg/day greater intake of phosphorus being associated with an increase of 0.03 mg/dL in serum phosphorus, after adjustment for confounders. The Panel notes that this represents about 1 % of the usual serum phosphorus concentration. A smaller study conducted in Spain showed no association between dietary phosphorus intake and serum phosphorus concentrations (Mataix et al., 2006). A possible explanation for these weak and inconsistent findings is that the renal handling of ingested phosphorus is so finely regulated that fasting serum phosphorus concentrations show only minimal modifications even in the presence of wide variations in intake. In most observational studies, serum phosphorus was measured only in fasting morning samples, while detailed feeding studies showed that changes in the order of 0.5–1.0 mg/dL in serum phosphorus related to phosphorus loading or restriction may be detected only by serial measurements of serum phosphorus throughout the day and subsequent average of the concentrations measured throughout the 24 hours (Portale et al., 1987; Calvo et al., 1988; Kemi et al., 2006). In particular, in six healthy men, a 40 % reduction in the 24-hour mean serum concentration of phosphorus as compared to the normal phosphorus intake (1 500 mg/day) occurred, during severe phosphorus restriction (500 mg/day for 10 days), while a 14 % increase in the 24-hour mean serum concentration of phosphorus was observed during phosphorus loading (3 000 mg/day for 10 days). Fasting serum phosphorus concentrations were unmodified during both restriction and loading periods as compared to the control period (Portale et al., 1987).

The Panel notes that serum phosphorus concentration cannot be considered as a reliable marker of intake as it increases for a short period after ingestion of a meal and then decreases and remains within a relatively narrow range due to homeostatic mechanisms. Moreover, because of fine renal regulation, fasting serum phosphorus concentrations show only minimal modifications even in the presence of wide variations in intake.

2.4.1.2. Urinary phosphorus excretion

Under normal conditions, the main excretory route of phosphorus from the body is through the kidney (see Section 2.3.6.1). Although urinary phosphorus excretion generally reflects dietary intake, it is regulated by a number of factors which limits its use as biomarker of intake.

2.4.2. Biomarkers of status

2.4.2.1. Serum phosphorus concentration

Serum inorganic phosphorus is the most commonly used indicator of phosphorus status; however, it generally inadequately reflects body stores. Only 1 % of total body phosphorus is found in extracellular fluid, and serum inorganic phosphorus concentrations typically range from 0.8–1.5 mmol/L in adults (Greenberg et al., 1960; IOM, 1997), irrespective of dietary phosphorus intake or whole body phosphorus content/status. Serum phosphorus concentrations are influenced by age, sex, lactation, diurnal and seasonal variations, vitamin D status, and pathological conditions such as malabsorption syndromes and insulin-dependent diabetes mellitus (Gibson, 2005).

2.4.2.2. Urinary phosphorus concentration

Urinary phosphorus concentration generally reflects dietary intake under normal conditions, as urine is the main excretory route. However, concentrations are affected by a whole range of other factors which impact on calcium and phosphorus metabolism (see Section 2.3.6.1). Therefore, urinary phosphorus is of limited use as biomarker of phosphorus status.

2.4.2.3. Serum parathyroid hormone (PTH)

PTH is the most important endocrine regulator of calcium and phosphorus concentrations in extracellular fluid. It is secreted from the parathyroid glands and its major sites of action are bone and kidney. However, this hormone is of limited use as a biomarker as its concentration is affected by vitamin D status, serum calcium and phosphorus concentrations.

2.4.2.4. Other biomarkers

Besides PTH, other phosphorus regulating factors, such as FGF-23 and Klotho, a protein present both in transmembrane and in circulating form and needed for FGF-23 to bind to its receptor, have recently been suggested as possible biomarkers of phosphorus status (see Gutierrez (2013)). In particular, FGF-23, along with PTH, regulate the reabsorption of phosphorus at the level of the renal proximal tubule. Studies in healthy volunteers showed that the secretion of FGF-23 reacts to variation in dietary phosphorus intake, increasing under conditions of excess dietary intake and being reduced by dietary phosphorus restriction (Oliveira et al., 2010; Moe et al., 2011; Shigematsu et al., 2012). Other studies indicated that Klotho may independently contribute to regulate renal phosphorus handling (Hu et al., 2010). The possible role of these factors as novel biomarkers of phosphorus status is still unclear.

2.4.2.5. Conclusions on biomarkers of phosphorus intake and status

The Panel concludes that there is currently no reliable biomarker of phosphorus intake and status.

2.5. Effects of genotypes

Understanding of phosphorus homeostasis has largely been obtained from molecular studies of human genetic disorders (Bergwitz and Juppner, 2010) including both inherited and acquired disorders (Christov and Jüppner, 2013). Hereditary diseases in phosphorus metabolism and the cloning of the

genes leading to these disorders (including urinary phosphate wasting and depletion of phosphorus stores (Alizadeh Naderi and Reilly, 2010)) have provided understanding of the regulation of phosphorus metabolism in both healthy and diseased individuals and have shown that the osteo-renal metabolic axis plays a large role in phosphorus homeostasis (de Menezes et al., 2006).

Genetic disorders which affect urinary excretion of phosphorus have a major impact on serum phosphorus concentrations. For example, mutations in genes such as NPT2 and PiT encoding phosphate transporters lead to disturbed phosphorus homeostasis (Prié and Friedlander, 2010). Additionally, hypophosphataemia and hypophosphataemic rickets are caused by mutations in the sodium-phosphate co-transporters NaPi-IIa and NaPi-IIc, respectively (Jüppner, 2007; Pettifor, 2008; Ramasamy, 2008). Elucidation of these mechanisms has identified regulators of phosphorus homeostasis including FGF-23 and a phosphate-regulating gene with homologies to endopeptidases on the X-chromosome (PHEX) (Tenenhouse, 2005).

The Panel notes that, although genetic defects leading to a number of rare inherited or acquired disorders affecting phosphorus homeostasis have been characterised at the molecular level, no genotypes have been identified that would require consideration in the estimation of DRVs for phosphorus in the general population.

3. Dietary sources and intake data

3.1. Dietary sources

Phosphorus is found in many foods. The major dietary contributors to phosphorus intake are foods high in protein content, i.e. milk and milk products (approximately 20–30 %) followed by meat, poultry and fish, grain products and legumes (Calvo and Uribarri, 2013).

Currently, calcium glycerophosphate, calcium salts of orthophosphoric acid, ferric sodium diphosphate, ferrous ammonium phosphate, ferric diphosphate (ferric pyrophosphate), magnesium glycerophosphate, magnesium salts of orthophosphoric acid, manganese glycerophosphate, sodium salts of orthophosphoric acid, potassium glycerophosphate, potassium salts of orthophosphoric acid, riboflavin 5′-phosphate (sodium) and pyridoxine 5′-phosphate may be added to both foods[6] and food supplements,[7] whereas ferrous phosphate, sodium monofluorophosphate, thiamine monophosphate chloride, thiamine pyrophosphate chloride, and pyridoxal 5′-phosphate may only be used in food supplements.[6] The phosphorus content of infant and follow-on formulae[8] is regulated.

The use by the food industry of food additives containing phosphorus is widespread. Most phosphorus-containing additives are inorganic salts of phosphorus that are widely used in the processing of many different foods, ranging from baked goods and restructured meats to cola beverages. However, the amount of phosphorus contributed by the use of phosphorus-containing food additives in processed and prepared foods is difficult to quantify (Calvo and Uribarri, 2013). Data on phosphorus in food composition databases likely underestimate the contribution from phosphate-containing additives (Oenning et al., 1988). This is partly due to changes in phosphorus content as the processing and formulation of new food products evolves. The ability to accurately capture dietary intakes is related to the food coverage in the database and the proportion of values based on chemical analysis as well as to the dietary assessment method used. It has been estimated that phosphorus added during processing can represent an average daily intake of 500 mg/day in the US, ranging from 300 mg/day to 1 000 mg/day depending on individual food preferences (IOM, 1997).

[6] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods, OJ L 404, 30.12.2006, p. 26

[7] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements, OJ L 183, 12.7.2002, p. 51

[8] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC, OJ L 401, 30.12.2006, p.1.

3.2. Dietary intake

EFSA estimated dietary intakes of phosphorus from food consumption data from the EFSA Comprehensive Food Consumption Database (EFSA, 2011b), classified according to the food classification and description system FoodEx2 (EFSA, 2011a). Data from 13 dietary surveys in nine EU countries were used. The countries included were Finland, France, Germany, Ireland, Italy, Latvia, the Netherlands, Sweden and the UK. The data covered all age groups from infants to adults aged 75 years and older (Appendix A).

Nutrient composition data for phosphorus were derived from the EFSA Nutrient Composition Database (Roe et al., 2013). Food composition information of Finland, France, Germany, Italy, the Netherlands, Sweden and the UK were used to calculate phosphorus intakes in these countries, assuming that the best intake estimate would be obtained when both the consumption data and the composition data are from the same country. For nutrient intake estimates of Ireland and Latvia, food composition data from the UK and Germany, respectively, were used, because no specific composition data from these countries were available. In case of missing values in a food composition database, data providers had been allowed to borrow values from another country's database. The amount of borrowed phosphorus values in the seven composition databases used varied between 15 and 85 %. Estimates were based on food consumption only (i.e. without dietary supplements). Nutrient intake calculations were performed only on subjects with at least two reporting days.

Data on infants were available from Finland, Germany, the UK, and Italy. The contribution of human milk was taken into account if the amounts of human milk consumed (Italian INRAN SCAI survey and the UK DNSIYC survey) or the number of breast milk consumption events (German VELS study) were reported. In case of the Italian INRAN SCAI survey, human milk consumption had been estimated based on the number of eating occasions using standard portions per eating occasion. In the Finnish DIPP study only the information "breast fed infants" was available, but without any indication about the number of breast milk consumption events during one day or the amount of breast milk consumed per event. For the German VELS study, the total amount of breast milk was calculated based on the observations by Paul et al. (1988) on breast milk consumption during one eating occasion at different ages, i.e. the amount of breast milk consumed on one eating occasion was set to 135 g/eating occasion for infants aged 6–7 months and to 100 g/eating occasion for infants aged 8–12 months. The Panel notes the limitations in the methods used for assessing breast milk consumption in infants (Appendices B and C) and related uncertainties in the intake estimates for infants.

Average phosphorus intakes ranged between 265 and 531 mg/day (102–154 mg/MJ) in infants (aged between 1 and 11 months, four surveys), between 641 and 973 mg/day (149–207 mg/MJ) in children aged 1 to < 3 years (five surveys), between 750 and 1 202 mg/day (133–206 mg/MJ) in children aged 3 to < 10 years (seven surveys), between 990 and 1 601 mg/day (131–196 mg/MJ) in children aged 10 to < 18 years) (seven surveys), and between 1 000 and 1 767 mg/day (149–207 mg/MJ) in adults (≥ 18 years) (eight surveys). Average daily intakes were in most cases slightly higher in males (Appendix B) compared to females (Appendix C) mainly due to larger quantities of food consumed per day.

The main food group contributing to phosphorus intakes were milk and dairy products and grains and grain-based products. In children and adults, milk and dairy products contributed up to about 30–53 % to phosphorus intake in the different age classes. Grains and grain-based products contributed up to 27–38 % to phosphorus intake. The contribution of meat and meat products was between 10 and 25 % in the age groups from 10 years and above. Differences in main contributors to phosphorus intakes between sexes were minor (Appendix D and E).

EFSA's phosphorus intake estimates in mg/day were compared with published intake values, where available, from the same survey and dataset and the same age class using the German EsKiMo and VELS surveys in children (Kersting and Clausen, 2003; Mensink et al., 2007), the study in Finnish adolescents (Hoppu et al., 2010), the French national INCA2 survey (Afssa, 2009), the Irish NANS (IUNA, 2011), the FINDIET 2012 Survey (Helldán et al., 2013), the Italian INRAN-SCAI Survey

(Sette et al., 2011), the Dutch National Dietary Survey (van Rossum et al., 2011), and the Swedish national survey Riksmaten (Amcoff et al., 2012) (Table 2).

Table 2: EFSA's average daily phosphorus intake estimates, expressed as percentages of intakes reported in the literature

Country	% of published intake (% range over different age classes in a specific survey)
Finland	99–100 (Finnish adolescents), 91–93 (FINDIET 2012)
France	97–102 (INCA2)
Germany	80–83 (VELS infants), 92–102 (VELS children), 106–111 (EsKiMo)
Ireland	109–115 (NANS)
Italy	97–102 (INRAN-SCAI)
NL	91–93 (Dutch National Dietary Survey)
Sweden	106–112 (Riksmaten)

When the EFSA phosphorus intake estimates were compared with published intake estimates from the same surveys and same age ranges, the EFSA estimates differed up to about 10 % from the published values in four countries (Finland, France, Italy, and the Netherlands) and in Germany, except among infants in the German VELS study, where the EFSA intake estimates were lower by 17–20 % compared to published values. One reason for the difference in the intake estimates for VELS seems to be the phosphorus content of the infant- and follow-on formulas in the composition databases. For the EFSA intake estimates the unlikely high phosphorus content of the German formula products were harmonised to comply with the legislation. When calculating the intake before and after this change, the underestimation in the phosphorus intakes increases from < -5 % to about -20 %.

For the Irish and Swedish surveys the EFSA intake estimates were higher by about 6–15 % compared to the published values. Overestimation of phosphorus intakes in Ireland may be partly related to the fact that the UK composition database was used, which is not fully compatible to the Irish situation. In addition, the Irish composite dishes were highly disaggregated to their ingredients in the data set submitted to EFSA.

Overall, several sources of uncertainties may contribute to these differences, including inaccuracies in mapping food consumption data according to food classifications and in nutrient content estimates available from the food composition tables, the use of borrowed phosphorus values from other countries in the food composition database, and replacing missing phosphorus values by values of similar foods or food groups in the phosphorus intake estimation process. As the intake calculations rely heavily on estimates of both food composition and food consumption, it is not possible to conclude which of these intake estimates would be closer to the actual phosphorus intakes.

4. Overview of Dietary Reference Values and recommendations

4.1. Adults

The Nordic countries considered that 400 mg/day of phosphorus is adequate for adults to maintain a plasma concentration of 0.8 mmol/L. Taking into account the PRIs set by IOM (1997) and SCF (1993), and taking the view that phosphorus intakes should correspond on a molar basis with those of calcium, a recommended intake of 600 mg/day had been set earlier (NNR, 2004). For the 5th edition of the Nordic Nutrition Recommendations (NNR 2012), it was considered that there are no new data indicating that these values should be changed (Nordic Council of Ministers, 2014).

The German-speaking countries (D-A-CH, 2013) considered that the data from which recommended intakes could be derived are much rarer for phosphorus than for calcium. An average requirement for adults was estimated at 580 mg/day following IOM (1997). Given a coefficient of variation (CV) of 10 %, the recommended intake was set at 700 mg/day.

The French Food Safety Authority (Afssa, 2001) used a factorial approach to calculate the Average Requirement (AR). Urinary and faecal losses were estimated according to Wilkinson (1976); Nordin B.E.C. (1989); Lemann (1996). For absorption efficiency in adults a mean value of 65 % was used (Wilkinson, 1976; Guéguen, 1982). Using a CV of 15 % the PRI for adults was calculated to be 750 mg/day.

The US Institute of Medicine (IOM, 1997) used the lower end of the normal adult serum inorganic phosphorus range (0.87 mmol/L) and considered that this value is obtained by an intake of ~580 mg (~19 mmol)/day (Nordin B.E.C., 1989), which was considered to be the best available Estimated Average Requirement (EAR) for adults. The extrapolation from absorbed intake to ingested intake was based on an absorption efficiency for phosphorus of 60–65 % (Stanbury, 1971; Wilkinson, 1976; Heaney and Recker, 1982). A CV of 10 % was used to determine a Recommended Dietary Allowance (RDA) of 700 mg (22.6 mmol)/day for adult men and women of all ages.

The SCF (1993) suggested that phosphorus intakes should correspond on a molar basis with those for calcium, and rounded values for AR and PRI were proposed accordingly.

The Netherlands Food and Nutrition Council (1992) was unable to set a minimum requirement on the basis of the data available at that time, but estimated for adults that the minimum requirement was no higher than 400 mg/day (Marshall et al., 1976). However, an adequate range of intake was set by relating the phosphorus requirement to the calcium requirement, which was revised, though, in the year 2000 (Health Council of the Netherlands, 2000). In 1992, in light of animal experiments (FAO/WHO, 1974; Schaafsma, 1981), it was considered that a calcium/phosphorus ratio (weight by weight) of less than 0.5 should be avoided. It was suggested to apply the lower limit of the RDA for calcium as the lower limit of the adequate range of phosphorus intake. Allowing for a calcium/phosphorus ratio of 0.5 (weight by weight), the upper limit of the adequate range for phosphorus intake was set at twice the lower limit of the RDA for calcium. As kidney function gradually declines as ageing progresses (Rowe et al., 1976), it was stated that regulation of phosphate balance in older adults on a phosphate rich diet may be accompanied by chronic low level stimulation of the parathyroid, which in the long term can promote bone decalcification. Therefore, the upper limit of the adequate range of phosphorus intake for adults over 50 years was calculated on the basis of a calcium/phosphorus ratio (weight by weight) of 0.7. The lower limit was equated with that of adults up to the age of 50 years.

The UK COMA (DH, 1991) took the view that requirements should be set at a ratio of 1 mmol phosphorus: 1 mmol calcium as they are present in the body in equimolar amounts. Accordingly, the Reference Nutrient Intake (RNI) for phosphorus was set at the equimolar value of the calcium RNI.

An overview of DRVs for phosphorus for adults proposed by various committees can be found in Table 3.

779 **Table 3:** Overview of Dietary Reference Values for phosphorus for adults

	NCM (2014)	D-A-CH (2013)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) [(a)]	DH (1991)
Age (years)	18–20	≥ 19	20–64	≥ 19	≥ 18	19–50	≥ 19
PRI [(a)]							
Men (mg/day)	700	700	750	700	550	700–1400	550
Women (mg/day)	700	700	750 [(b)]	700	550	700–1400	550
Age (years)	≥ 21		65–74			≥ 50	
PRI							
Men (mg/day)	600		750			700–1150 [(d)]	
Women (mg/day)	600		800 [(c)]			700–1150 [(d)]	
Age (years)			≥ 75				
PRI							
Men (mg/day)			800				
Women (mg/day)			800				

780 NCM, Nordic Council of Ministers; NL, Netherlands' Food and Nutrition Council; PRI, Population Reference Intake
781 (a): Adequate range of intake
782 (b): 20–55 years
783 (c): > 55 years
784 (d): Lower limit of the adequate range of intake for adults below the age of 50 years is also considered adequate for this age
785 group

786 ## 4.2. Infants and children

787 The Nordic countries considered that recommended phosphorus intakes should correspond on a molar
788 basis with those for calcium (NNR, 2004). For the 5th edition of the NNR, it was considered that there
789 are no new data indicating that these values should be changed (Nordic Council of Ministers, 2014).

790 For puberty and adolescence the German-speaking countries (D-A-CH, 2013) considered the
791 requirement for phosphorus to be increased relative to the AR of adults because of new tissue
792 formation and bone growth. Accordingly, a recommended intake of 1 250 mg/day was set for children
793 and adolescents aged 10 to below 19 years of age.

794 Afssa (2001) proposed an Adequate Intake (AI) of 275 mg/day for infants aged 6–12 months, in line
795 with IOM (1997). For children, Afssa (2001) used a factorial approach to calculate the ARs. Allowing
796 for phosphorus content of bone (Fomon et al., 1982) and other tissues, values were derived from the
797 amount of calcium required during growth using a calcium:phosphorus ratio of the weight gain of 1:7
798 up to the age of 18 years, with the amount of phosphorus required for growth ranging from 50 mg/day
799 (age 1–3 years) to 150 mg/day (age 10–14 years). Urinary and faecal losses were estimated according
800 to Wilkinson (1976); Nordin B.E.C. (1989); Lemann (1996). For absorption efficiency, mean values of
801 70 % (age 15–18 years) to 75 % (age 1–14 years) were used in children and adolescents (Wilkinson,
802 1976; Guéguen, 1982). A CV of 15 % was used to derive the PRIs.

803 For infants aged zero to six months, IOM (1997) set an AI of 100 mg (3.2 mmol)/day based on a mean
804 breast milk intake of 780 mL/day (Butte et al., 1984a; Allen et al., 1991) and an average phosphorus
805 concentration of human milk of 124 mg/L (Atkinson et al., 1995). For infants aged 6–12 months, the
806 AI of 275 mg (8.9 mmol)/day was based on the phosphorus intake from breast milk and solid foods.
807 An average intake of 75 mg/day was calculated from an average human milk concentration of
808 124 mg/L (Atkinson et al., 1995) and a mean breast milk intake of 600 mL/day (Dewey et al., 1984).
809 The contribution from solid foods was estimated to be 200 mg/day from data on 40 infants fed
810 standard infant formula and solid food (Specker et al., 1997), which was comparable to estimations
811 from the 1976–1980 NHANES II for infants aged 7–12 months (Montalto and Benson, 1986). For
812 children aged 1–3 years, an EAR of 380 mg (12.3 mmol)/day was based on a factorial estimate[9].

[9] EAR = (accretion + urinary loss)/ fractional absorption

Accretion of phosphorus for bone and lean tissue was estimated to be 54 mg (1.74 mmol)/day calculated from balance studies in children aged 4–12 years (Fomon et al., 1982) corrected to the average weight gain for children aged 1–3 years. A value of 19 % by weight was used as the phosphorus content of bone. The phosphorus content of lean tissue was assumed to be 0.23 % based on known composition of muscle (Pennington, 1994). The urinary loss was calculated to be 21.3 mg (6.9 mmol)/day using the equation developed by Lemann (1996). A conservative estimate for efficiency of phosphorus absorption of 70 % was used as suggested for children aged 9–18 years (Lemann, 1996). As the variation in requirements could not be determined, a CV of 10 % was assumed, which resulted in an RDA of 460 mg (14.8 mmol)/day. For children aged 4–8 years an EAR of 405 mg (13.1 mmol)/day was derived using the same factorial approach as for ages 1–3 years. In calculating the accretion of phosphorus over this age interval, it was considered that there were no great differences between 4–6 and 6–8 years of age. An accretion value of 62 mg (0.2 mmol)/day was derived. The assumptions for efficiency of phosphorus absorption and urinary loss of phosphorus are identical to that used for 1–3 years. The RDA for children aged 4–8 years was set at 500 mg (16.1 mmol)/day using a CV of 10 %. As there are few balance studies in children aged 9–18 years, the same method of estimation by tissue accretion was used. Bone and lean mass accretion was estimated using three studies (Deurenberg et al., 1990; Slemenda et al., 1994; Martin et al., 1997). Assuming a phosphorus content of bone of 19 % and a phosphorus content of soft tissue of 0.23 % (Pennington, 1994), daily phosphorus needs during peak growth would approximate 200 mg (6.5 mmol) for boys and 150 mg (4.8 mmol) for girls. Urinary loss of phosphorus was calculated using the equation from Lemann (1996) to 565 mg (18.2 mmol)/day. Absorption efficiency was averaged to 60–80 % (Lutwak et al., 1964; Greger et al., 1978), and a mid point of 70 % was used. An EAR of 1 055 mg (34 mmol)/day for both girls and boys was set; thus, with an assumed CV of 10 % the RDA was set at 1 250 mg (40.3 mmol)/day for ages 9–18 years.

The SCF (1993) suggested that phosphorus intakes should correspond on a molar basis with those for calcium and rounded PRI values were proposed accordingly.

The Netherlands Food and Nutrition Council (1992) set an adequate range of intake derived from the lower limit of the adequate range of intake for calcium and a recommended calcium:phosphorus ratio. For infants aged 6–12 months a calcium/phosphorus ratio (weight by weight) of 1.0 was applied, whereas the calcium/phosphorus ratio was 0.5–1.0 (weight by weight) for children and adolescents.

The UK COMA (DH, 1991) took the view that requirements should be set at a molar calcium:phosphorus ratio of 1 as they are present in the body in equimolar amounts. Accordingly, the RNI for phosphorus was set at the equimolar value of the calcium RNI.

An overview of DRVs for phosphorus for infants and children proposed by various committees can be found in Table 4.

848 **Table 4:** Overview of Dietary Reference Values for phosphorus for children from 4 months

	NCM (2014)	D-A-CH (2013)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) [a]	DH (1991)
Age (months)	6–11	4–<12	6–12	7–12	6–11	6–12	0–12
PRI (mg/day)	420	300	275 [b]	275 [b]	300	400	400
Age (years)	1–5	1–<4	1–3	1–3	1–3	1–4	1–3
PRI (mg/day)	470	500	360	460	300	400–800	270
Age (years)		4–<7	4–6	4–8	4–6	4–7	4–6
PRI (mg/day)		600	450 [c]	500	350	400-800	350
Age (years)	6–9	7–<10	7–9		7–10	7–10	7–10
PRI (mg/day)	540	800	600 [c]		450	600–1 200	450
Age (years)	10–17	10–<19	10–12	9–18	11–17	10–16	11–18
PRI							
Boys (mg/day)	700	1 250	830	1 250	775	900–1 800	775
Girls (mg/day)	700	1 250	800	1 250	625	700–1 400	625
Age (years)			16–19			16–19	
PRI							
Boys (mg/day)			800			800–1 600	
Girls (mg/day)			800			700–1 400	

849 NCM, Nordic Council of Ministers; NL, Netherlands' Food and Nutrition Council; PRI, Population Reference Intake
850 (a): Adequate range of intake
851 (b): Adequate Intake (AI)
852 (c): As reported on page 507 of the report
853

854 ### 4.3. Pregnancy

855 The German-speaking countries (D-A-CH, 2013) estimated that during pregnancy an average of
856 60 mg/day of phosphorus must be provided to meet the needs of pregnancy. Taking into account
857 intestinal absorption an additional allowance of 100 mg/day was set compared to that for non-pregnant
858 women.

859 Afssa (2001) used a factorial approach to estimate the AR. A full term infant contains about 17 g of
860 phosphorus (Fomon et al., 1982), indicating a mean retention of 150 mg/day during the last trimester
861 of pregnancy. For absorption efficiency mean values of 70–75 % were used for pregnant women
862 (Wilkinson, 1976; Guéguen, 1982). An intake of 800 mg/day was recommended taking into account
863 inevitable bone loss and subsequent compensation.

864 The IOM (1997) considered that there was no evidence to support an increase in the EAR for pregnant
865 women above that of non-pregnant women. It was noted that intestinal absorption increases by about
866 10 % during pregnancy (Heaney and Skillman, 1971), which was considered sufficient to provide the
867 necessary phosphorus for fetal growth.

868 The Netherlands Food and Nutrition Council (1992) calculated an increased requirement of
869 100 mg/day during pregnancy based on the amount of phosphorus stored in the fetus.

870 The SCF (1993) and the UK COMA (DH, 1991) gave no increment for pregnant women compared to
871 the DRV for non-pregnant women.

872 An overview of DRVs for phosphorus for pregnancy proposed by various committees can be found in
873 Table 5.

874 **Table 5:** Overview of Dietary Reference Values for phosphorus for pregnant women

	NCM (2014)	D-A-CH (2013)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) [a]	DH (1991)
Age (years)		< 19		14–18			
PRI (mg/day)	700	1 250	800 [b]	1 250	550	800–1 600	550
Age (years)		≥ 19		19–50			
PRI (mg/day)		800		700			

875 NCM, Nordic Council of Ministers; NL, Netherlands' Food and Nutrition Council; PRI, Population Reference Intake
876 (a): Adequate range of intake
877 (b): Third trimester

878 ### 4.4. Lactation

879 D-A-CH (2013) estimated that an additional amount of phosphorus of 90–120 mg/day was needed
880 during lactation. Taking into account intestinal absorption an additional allowance of 200 mg/day was
881 set compared to that for non-lactating women.

882 Afssa (2001) used the factorial approach to derive the AR for lactation. It was estimated that
883 120 mg/day of phosphorus is secreted via breast milk, based on an average breast milk concentration
884 of 150 mg/L and a daily volume of milk secretion of 800 mL. The maintenance needs during lactation
885 were estimated at 350 mg/day and, considering an absorption efficiency of 65 % (as for non-lactating
886 adults) (Wilkinson, 1976; Guéguen, 1982) and a CV of 15 %, the PRI would have been 930 mg/day.
887 However, Afssa selected the value of 850 mg/day to take into account the normal variation of bone
888 stores (i.e. the obligatory loss of bone mass during pregnancy and lactation and their restauration
889 afterwards). The corresponding AR is 720 mg/day. An AR of 690 mg/day and a PRI of 850 mg/day
890 were also set for an equal number of months following breastfeeding to restore bone phosphorus
891 reserves.

892 The IOM (1997) stated that there was no evidence to support an increase in phosphorus requirement
893 during lactation. Apparently, increased bone resorption and decreased urinary excretion of phosphorus
894 (Kent et al., 1990) which occur independent of dietary intake of phosphorus or calcium, provide the
895 necessary phosphorus for milk production. Therefore, the EAR and RDA were estimated to be similar
896 to those set for non-lactating women of the respective age groups.

897 The SCF (1993) suggested that phosphorus intakes should correspond on a molar basis with those for
898 calcium and a rounded PRI value was proposed accordingly.

899 The Netherlands Food and Nutrition Council (1992) assumed an increased phosphorus need of
900 200 mg/day, calculated on the basis of the phosphorus content in breast milk and an absorption
901 efficiency of 60 % (Spencer et al., 1984).

902 The UK COMA (DH, 1991) took the view that requirements should be set at a ratio of 1 mmol
903 phosphorus: 1 mmol calcium as they are present in the body in equimolar amounts. Accordingly, the
904 RNI for phosphorus was set at the equimolar value of the calcium RNI.

905 An overview of DRVs for phosphorus for lactation proposed by various committees can be found in
906 Table 6.

907 **Table 6:** Overview of Dietary Reference Values for phosphorus for lactating women

	NCM (2014)	D-A-CH (2013)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) [(a)]	DH (1991)
Age (years)		< 19		14–18			
PRI (mg/day)	900	1 250	850	1 250	950	900–1 800	+ 440
Age (years)		≥ 19		19–50			
PRI (mg/day)		900		700			

908 NCM, Nordic Council of Ministers; NL, Netherlands' Food and Nutrition Council; PRI, Population Reference Intake
909 (a): Adequate range of intake
910

911 # 5. Criteria (endpoints) on which to base Dietary Reference Values

912 ## 5.1. Indicators of phosphorus requirement

913 As stated in Section 2.4, the Panel considers that there is no suitable biomarker of phosphorus intake
914 or status that can be used for setting DRVs for phosphorus.

915 ## 5.2. Balance studies on phosphorus

916 Balance studies are based on the assumption that a healthy subject on an adequate diet maintains an
917 equilibrium or a null balance between nutrient intakes and nutrient losses: at this null balance, the
918 intake matches the requirement determined by the given physiological state of the individual. When
919 intakes exceed losses (positive balance), there is nutrient accretion that may be attributable to growth
920 or to weight gain, anabolism or repletion of stores; when losses exceed intakes (negative balance),
921 nutrient stores are progressively depleted resulting, in the long term, in clinical symptoms of
922 deficiency. When performed at different levels of intake, balance studies enable the quantification of
923 basal or obligatory losses by regression to zero. In addition to numerous methodological concerns
924 about accuracy and precision in the determination of intakes and losses (Baer et al., 1999), the validity
925 of balance studies for addressing requirements has been questioned: they might possibly reflect only
926 adaptive changes before a new steady state is reached (Young, 1986), or they might reflect only the
927 conditions for maintenance of nutrient stores in the context of a given diet and, consequently, the
928 relevance of the pool size for health still needs to be established for each nutrient (Mertz, 1987).

929 Few phosphorus balance studies are available as compared to other minerals, like calcium, partly
930 because phosphorus isotopes cannot be safely used for kinetic studies. Thus, the study of the
931 regulation of phosphorus homeostasis has often been considered as subordinate to that of calcium.
932 Phosphorus balance, like calcium balance, is maintained by intestinal absorption, renal excretion, and
933 bone accretion. However, there are important differences between phosphorus and calcium balance.
934 Dietary phosphorus, which grossly parallels dietary protein, is present in abundance in most foods; this
935 is in contrast to calcium, which is restricted to relatively few food groups. Dietary phosphorus is
936 absorbed more efficiently than dietary calcium. Thus, phosphorus absorption is not a limiting factor.

937 ### 5.2.1. Balance studies in adults

938 Roberts et al. (1948) evaluated phosphorus retention and losses in nine healthy postmenopausal
939 women (age 52–74 years). After 3–5 weeks on a habitual diet with replicated menus, phosphorus
940 balance was evaluated in two consecutive five-day balance periods. Mean phosphorus intake on self-
941 selected diets was 1 100 mg/day (range 891–1 403 mg/day). At intakes below 1 100 mg/day, all
942 balances were negative, between 1 100 and 1 400 mg/day no consistent trend was observed, while at a
943 phosphorus intake above 1 400 mg/day, positive balances were more frequent than negative balances.
944 However, the authors concluded that in this study the variation in individual responses to a given
945 amount of phosphorus intake was so high that phosphorus requirements could not be determined with
946 validity even at the individual level.

Ohlson et al. (1952) evaluated phosphorus balance in a multi-centre study in 136 women (30–85 years of age) on self-selected diets. No standardisation of the pre-balance period was performed. Phosphorus intake was highly variable, ranging from 490 to 1 700 mg/day, with a significant decrease of phosphorus intake with increasing age. Phosphorus balance was evaluated in one balance period (from 7 to 10 days). The prediction of phosphorus intake required for null balance (using a linear regression equation) was 1 250 mg/day from 30 to 39 years of age, 1 320 mg/day from 40 to 49 years, 1 420 mg/day from 50 to 59 years, 1 510 mg/day from 60 to 69 years and 1 130 mg/day from 70 to 79 years. The Panel notes that in this multicentre study a considerable degree of uncertainty exists with regard to study procedures, selection of the participants and standardisation of dietary intake.

Scoular et al. (1957) undertook a long-term balance study in 125 young women (17–27 years of age) on self-selected diets with a day-to-day variation in phosphorus intake ranging from 120 to 400 % of the daily intake suggested by the US National Research Council (NRC, 1953). Phosphorus intake was related to balance being positive or negative, but absolute values for balances were not given. The average total intake of phosphorus allowing a positive balance was 1 150 mg/day.

Marshall et al. (1976) concisely report about balance studies that aimed to evaluate calcium, magnesium and phosphorus requirements in adults. Participants were administered a constant diet for two weeks. Faeces and urine were collected from days 8 to 14. The final balance was the mean of the daily balances in the second week. Based on 646 balances, phosphorus balance was zero down to a phosphorus intake of 400 mg/day. The authors conclude that it is not possible to define phosphorus requirements based on these data.

In a balance study that aimed to evaluate the effect of phosphorus on the intestinal absorption of calcium (Spencer et al., 1978), 19 male subjects (average age 54 years, range 38–65 years) received, under metabolic ward conditions, up to five different levels of dietary calcium (from 200 to 2 700 mg/day) at up to two different levels of dietary phosphorus (800 mg/day and 2 000 mg/day). The diet was kept constant for several weeks or months prior to the start of the balance studies and throughout the study phases and was analysed for nitrogen, calcium, and phosphorus in each metabolic period. The minimum duration of each study period was 22 days and the duration of balance periods was six days. Phosphorus balance was positive or zero at each level of phosphorus and calcium intake.

Spencer et al. (1984) studied the effect of calcium on phosphorus metabolism in adult males, by determining phosphorus and calcium balances during three different levels of calcium intake of approximately 200, 800, and 2 000 mg/day. Each of these calcium intakes was given with two different intake levels of phosphorus of approximately 800 and 2 000 mg/day to 44 adult male subjects (aged 31–71 years). Participants had received a standard diet and a constant daily fluid intake under metabolic ward conditions for a minimum of three weeks before the start of the balance studies. In each metabolic period, aliquots of the diet were analysed. Negative phosphorus balance (-60 mg/day) was observed only during the low calcium (200 mg/day) and "normal" phosphorus (800 mg/day) diet period. Under all other dietary conditions, phosphorus balance was zero or positive. In particular, under "normal" calcium and phosphorus intake (defined as 800 mg/day), a slightly positive phosphorus balance was observed.

Mahalko et al. (1983) evaluated mineral utilisation by metabolic balance techniques in 10 healthy male volunteers fed diets containing 65 and 94 g protein/day. Both diets contained approximately 1 000 mg phosphorus/day. Mineral balances were measured on the last 12 days of each 28-day diet period and duplicate samples of the diet were analysed. Zero phosphorus balance was observed at both levels of protein intake.

Lakshmanan et al. (1984) assessed calcium and phosphorus balances in 13 men aged 22–49 years and in 16 women aged 20–53 years over a one-year-period, in which subjects consumed self-selected diets. An additional three men and two women participated in the study for one- to three-quarters of the year. Once every season the subjects collected duplicate food and beverage samples for one week; the phosphorus content of the diet was analysed, as was the phosphorus concentration in faeces and urine

collected during the week. Although the average daily intake of phosphorus was considered "adequate" (1 533 mg/day in men and 1 059 mg/day in women) the authors reported an unexpectedly high percentage (75 %) and extent of negative phosphorus balances (mean of all women: -130 mg/day; mean of all men: -239 mg/day) in these subjects consuming self-selected diets. The Panel considers that no conclusions can be drawn from this study due to the absence of an equilibration period with a standardised diet and metabolic ward conditions.

Spencer et al. (1994) evaluated balances of calcium, magnesium and phosphorus in five healthy males at two different intake levels of calcium (240 and 800 mg/day) and magnesium (about 250 and 800 mg/day). Dietary phosphorus was about 800 mg/day (range of means in four studies 765–858 mg/day). After an equilibration period of four weeks, six-day balance studies were performed under metabolic ward conditions. Phosphorus balances were positive (means from +16 to +38 mg/day) under all different dietary conditions.

Nishimuta et al. (2004) aimed to estimate the requirements of calcium, magnesium and phosphorus in Japanese adults. A total of 109 volunteers (23 males, 86 females), ranging from 18–28 years of age, took part in mineral balance studies whose duration ranged from 5 to 12 days, with 2 to 4 days of adaptation. Dietary menus were designed so as to meet dietary allowances in Japan. Dietary phosphorus intake (from duplicate diet analysis) ranged from 13.5 to 45.7 mg/kg body weight per day. No absolute balance data are reported. The mean value and upper limit of the 95 % confidence interval (CI) of the dietary intake of phosphorus when the balance of phosphorus was equal to zero were 22.6 and 24.1 mg/kg body weight per day, respectively. The Panel notes the short equilibration period in this study.

Nishimuta et al. (2012) evaluated the estimated equilibrated dietary intake, defined as the intercept of a linear regression equation between intake (*Y*) and balance (*X*), for nine essential minerals including phosphorus, using data from 13 studies of young women (n = 131, range 18–26 years) consuming a standard diet designed to meet dietary allowances in Japan. Before the balance period, a 2- to 4-day adaptation period took place, during which participants were given the experimental diets. Duplicate diet samples were obtained and analysed. Mean and median phosphorus balances were close to zero (mean, -0.18 ± 1.45 mg/kg body weight per day; median, -0.21 mg/kg body weight per day). The estimated equilibrated dietary intake for phosphorus was 17.2 mg/kg standard body weight[10] per day (95 % CI 16.7–17.8). This value was superimposable to the estimated dietary intake of phosphorus during the balance study (17.2 ± 3.1 mg/kg standard body weight per day). The Panel notes the rather short equilibration period in this study.

The Panel notes that the available phosphorus balance studies are rather heterogenous with regard to the population examined, the presence and duration of equilibration periods, the duration of balance periods, the level of phosphorus intake, and the intake of other dietary factors possibly affecting phosphorus metabolism, that only few studies were conducted under metabolic ward conditions and that zero phosphorus balance may be achieved across a wide range of intakes. The Panel notes the many limitations of these studies and considers that balance studies cannot be used for setting DRVs for phosphorus for adults.

5.2.2. Balance studies in children

Greger et al. (1978) assessed calcium, magnesium, phosphorus, copper and manganese balances in 14 girls (aged 12.5–14.5 years) during a 30-day period at two different levels of dietary zinc (7.4 or 13.4 mg zinc/day) and after a nine-day equilibration period. Dietary phosphorus intake was set at 850 mg/day (data from analysed diets). At this intake level, the participants were in slightly positive phosphorus balance.

[10] Body weight based on height and a BMI of 22 kg/m^2

The Panel notes that data are available from only one small study in female adolescents and considers that balance studies cannot be used for setting DRVs for phosphorus for children.

5.2.3. Balance studies in pregnancy

Ashe et al. (1979) evaluated the retention of calcium, iron, phosphorus and magnesium in 10 healthy pregnant white women consuming self-selected diets. A maximum of six seven-day balance periods were completed on each subject. Average calcium intake was 1 370 ± 290 mg/day. At an estimated phosphorus intake of 1 340 ± 280 mg/day, zero phosphorus balance was observed. The Panel notes that in this study under free-living conditions a very large intra- and inter-subject variation from one seven-day experimental period to another was observed.

The Panel considers that balance studies cannot be used for setting DRVs for phosphorus for pregnancy.

5.2.4. Calcium-to-phosphorus ratio in the diet

Several committees have set DRVs for phosphorus corresponding to those for calcium, either on a molar basis or on a weight basis. The importance of the molar ratio of calcium-to-available phosphorus during growth has been acknowledged (EFSA NDA Panel, 2014). In adults, there are findings suggesting that the balance in intake between these two minerals may have greater influence than the absolute intake of phosphorus. Animal studies (in rats, dogs, baboons, and other species) have shown that high phosphorus intake in combination with low calcium intake may contribute to secondary hyperparathyroidism, bone resorption, low peak bone mass, and increased bone fragility (reviewed in Calvo and Tucker (2013)). Cross-sectional studies suggest that the dietary calcium-to-phosphorus molar ratio is significantly associated with (site-specific) BMD and/or bone mineral content (BMC) (Teegarden et al., 1998; Brot et al., 1999; Ito et al., 2011) or indicators of bone metabolism (Kemi et al., 2008; Kemi et al., 2010). In some studies, the dietary calcium-to-phosphorus molar ratio was more closely related to both BMD and indicators of bone metabolism than the calcium or phosphorus intake *per se*. A mild phosphorus-induced secondary hyperparathyroidism could be considered a plausible mechanism for the association between a low dietary calcium-to-phosphorus molar ratio and lower BMD or BMC. The Panel notes, however, that other studies present conflicting evidence (Heaney and Recker, 1987; Heaney and Nordin, 2002).

Thus, the Panel considers that the data cannot be used to define a precise dietary calcium-to-available phosphorus molar ratio in adults for bone health, but notes that calcium and phosphorus are present in the body in approximately equimolar amounts (Section 2.3.7).

5.3. Phosphorus requirements in pregnancy and lactation

The role of dietary phosphorus during pregnancy and lactation has not been established. The Panel notes that no quantitative assessment of phosphorus resorption from bone during lactation is available. However, extended lactation is associated with a modest reduction in BMD, with a return to baseline values at 12 months after parturition (Sowers et al., 1993; Karlsson et al., 2001) independently of the length of lactation (Moller et al., 2012).

Prentice (2003) reviewed the evidence about biological adaptation mechanisms (increases in food intake, elevated gastro-intestinal absorption, decreased mineral excretion and mobilisation of tissue stores) required to preserve the maternal mineral economy while meeting the additional mineral requirements during pregnancy and lactation. The author concluded that pregnancy and lactation are associated with physiological adaptive changes in mineral metabolism that are independent of maternal mineral supply within the range of normal dietary intakes. These processes provide the minerals necessary for fetal growth and breast milk production without requiring an increase in maternal dietary intake or compromising maternal bone health in the long term.

5.4. Phosphorus intake and health consequences

A comprehensive search of the literature published between 1990 and September 2012 was performed as preparatory work to this assessment, to identify relevant health outcomes upon which DRVs for phosphorus may potentially be based (Eeuwijk et al., 2012). This literature search has been updated to cover the time from September 2012 until December 2014. The relationship between phosphorus intake and various health outcomes has been investigated in a number of observational studies, while intervention studies with phosphorus as a single nutrient are not available. In the absence of reliable biomarkers of phosphorus intake and status (Section 2.4), only studies on phosphorus intake will be considered for this section, though the Panel notes the difficulty in assessing phosphorus intake (Section 3.1).

5.4.1. Bone health

Prospective studies report on the association between phosphorus intake and bone health in children. In three studies maternal phosphorus intake during pregnancy and bone mass of the child were studied. In one study diet and lifestyle factors in children in relation to their bone mass were studied.

Jones et al. (2000) and Yin et al. (2010) reported on the association between maternal phosphorus intake and bone mass in children in the same prospective cohort study in Tasmania, Australia. Jones et al. (2000) investigated bone mass in children at age eight years. Yin et al. (2010) investigated bone mass in the same population at age 16 years. Maternal dietary intake during the third trimester of pregnancy was measured using a self-administered FFQ. Phosphorus density of the maternal diet (mg/kcal or MJ) was calculated by dividing estimated daily phosphorus intake by the estimated total daily energy intake. At age eight and 16 years dual-energy X-ray absorptiometry (DXA) scans were performed. As not all children in the cohort underwent a scan at both eight and 16 years of age, the populations described in the studies of Jones et al. (n = 173) and Yin et al. (n = 216) are not identical. Mean maternal phosphorus intake during the third trimester of pregnancy was 2 767 (SD 1 655) mg/day (Jones et al., 2000) and 2 314 (SD 898) mg/day (Yin et al., 2010). At age eight years, BMD of the femoral neck and lumbar spine were positively associated ($p = 0.01$ and $p = 0.001$) with phosphorus density of the maternal diet. Total body BMD was not associated with phosphorus density of the maternal diet ($p = 0.054$). At age 16 years, none of the BMD measures were associated with maternal phosphorus intake. In both studies, regression models were adjusted for children's current calcium intake. The Panel notes that the children who took part in this study were originally selected on the basis of having a higher risk of sudden infant death syndrome, that adjustments for multiple comparisons were not performed and that the self-reported maternal intake of protein, calcium, magnesium and phosphorus was very high, and much higher than in Australian pregnant women (Hure et al., 2009) and compared to Australian recommended intakes (NHMRC, 2005).

Tobias et al. (2005) studied the relationship between maternal diet during pregnancy, evaluated by an FFQ, and bone mass in childhood in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort in the UK. Data from 4 451 mother-child pairs were analysed. Mean maternal phosphorus intake during pregnancy was 1 339 (SD 338) mg/day, which is comparable to the mean daily intake of 1 112 (SD 299) mg/day measured in women in the UK (Henderson et al., 2003). Bone mineral mass of the children was measured at nine years of age. At multivariate analysis, including other maternal dietary factors, intake of phosphorus during pregnancy was not associated with measures of bone density in children ($p = 0.128$). Analyses were not adjusted for children's intakes of calcium or other micro- or macronutrients.

Bounds et al. (2005) evaluated the association between diet and lifestyle factors and bone mineral indices in a cohort of 52 children. Dietary intake was assessed at nine collection points (from 2.3 to eight years of age) by means of in-home dietary interviews. During eight years of follow-up, dietary data and data on sedentary activities (i.e. time not spent in physical activity) of the children were collected. Bone mineral indices were measured by a DXA scan when children were eight years old. Correlations between phosphorus intake and BMC ($r = 0.33$) and BMD ($r = 0.30$) were significant ($p < 0.05$). In a multivariate regression model predicting BMC at eight years, phosphorus intake

showed a small but significant contribution to the model ($\beta = 0.11$; $R^2 = 0.05$; $p = 0.01$). However, calcium or other micro- or macronutrients were not included in the regression model.

The Panel notes that there is some indication that maternal intake of phosphorus during pregnancy may be associated with the BMD of the femoral neck and lumbar spine, but not total body BMD in the offspring at age eight years and that phosphorus intake during childhood may be associated with BMD at the age of eight years. The Panel notes, however, the many limitations of these studies.

The Panel considers that measures of bone health cannot be used to derive DRVs for phosphorus during pregnancy and in children.

5.4.2. Cancer

Few prospective studies have evaluated the association between dietary phosphorus intake and some types of cancer. The World Cancer Research Fund included phosphorus among the exposures for which the data were either of too low quality, too inconsistent, or the number of studies too few to allow conclusions to be reached on an association with cancer (WCRF/AICR, 2007).

5.4.2.1. Prostate cancer

Chan et al. (2000) prospectively evaluated the association between dietary phosphorus intake, assessed by self-administered FFQ, and prostate cancer in 27 062 Finnish male smokers included in the Alpha-Tocopherol Beta-Carotene Cancer Prevention (ATBC) Study. No significant independent associations of phosphorus and calcium intake and prostate cancer risk were observed. Men with lower calcium and higher phosphorus intake had a multivariate relative risk (RR) of 0.6 (95 % CI 0.3–1.0) compared to men with lower intakes of both nutrients, after adjustment for age, smoking, body mass index, total energy intake, education, and supplementation group, thus suggesting a possible interaction between the two nutrients.

Kesse et al. (2006) prospectively evaluated the association between dietary phosphorus intake, measured by at least five 24-hour records in the first 18 months of the study, and prostate cancer in 2 776 men of the SU.VI.MAX trial (SUpplémentation en VItamines et Minéraux Anti-oXydants). In almost eight years of follow-up 69 incident cases of prostate cancer occurred in the study population. A weak positive association between phosphorus intake and prostate cancer was observed ($p_{trend} = 0.04$), with a non-significant RR of 1.83 (95 % CI 0.89–3.73) comparing the highest versus the lowest quartile.

Tseng et al. (2005) prospectively evaluated the association between dietary phosphorus intake and prostate cancer in 3 612 men from the National Health and Nutrition Examination Epidemiologic Follow-up Study. Dietary intake was assessed by FFQ. After almost eight years of follow-up, there were 131 new cases of prostate cancer in the population. No association between phosphorus intake and prostate cancer risk was found in the fully adjusted regression model including calcium intake (RR for the highest tertile of phosphorus intake compared with the lowest tertile was 0.9 (95 % CI 0.5–1.6), $p_{trend} = 0.77$).

5.4.2.2. Other types of cancer

Michaud et al. (2000) examined the relationship between intakes of macro- and micronutrients and the risk of bladder cancer among men in the prospective Health Professionals Follow-Up Study. Dietary intake was assessed by FFQ. During 12 years of follow-up, 320 cases of bladder cancer were diagnosed in a population of 47 909 men. Phosphorus intake was not associated with incidence of bladder cancer ($p_{trend} = 0.40$). The multivariate adjusted RR (not adjusted for calcium) of the highest quintile (median 1 728 mg/day) compared with the lowest quintile (median 1 101 mg/day) was 0.85 (95 % CI 0.57–1.21).

Kesse et al. (2005) investigated the association between phosphorus intake and risk of colorectal adenoma and cancer among women in the French component of the European Prospective

Investigation into Cancer and Nutrition (E3N-EPIC) prospective study. Dietary data were collected using an FFQ. After follow-up of 3.7 years, 516 women were diagnosed with adenomas and 4 804 women were free of polyps, being confirmed by colonoscopy. For the colorectal cancer study, after a follow-up of 6.9 years, 172 cases of colorectal cancer were identified, while 67 312 women were free of the disease. A higher phosphorus intake was associated with a decreased risk of adenomas (p_{trend} = 0.005). The RR of the highest quartile (median phosphorus intake > 1 634 mg/day) compared with the lowest quartile (median < 1 412 mg/day) of intake was 0.70 (95 % CI 0.54–0.90). In a subgroup of women with high-risk adenomas no association was observed. This subgroup (n = 175) covered women diagnosed with large adenomas (> 1 cm in diameter), adenomas with severe dysplasia, multiple adenomas (≥ 3), and those with a villous component. No significant association between phosphorus intake and colorectal cancer was found.

5.4.2.3. Conclusions on cancer-related outcomes

The Panel considers that evidence of an association between phosphorus intake and cancer-related outcomes is inconsistent, and that available data on such outcomes cannot be used as a criterion for deriving DRVs for phosphorus.

5.4.3. Cardiovascular disease-related outcomes and all-cause mortality

Some observational studies are available that evaluated the association between phosphorus intake and cardiovascular disease (CVD).

Chang et al. (2014) prospectively investigated the association between phosphorus intake and mortality in 9 686 adults aged 20–80 years without diabetes, cancer, or kidney or CVD participating in NHANES III (1988–1994). Dietary phosphorus intake, assessed by 24-hour dietary recall, was expressed as the absolute intake and phosphorus density (phosphorus intake divided by energy intake). Median follow-up time was 14.7 years. In analyses adjusted for demographics, cardiovascular risk factors, kidney function, and energy intake (not adjusted for calcium intake), higher phosphorus intake was associated with higher all-cause mortality in individuals who consumed > 1 400 mg/day [adjusted hazard ratio (HR) (95 % CI) 2.23 (1.09–4.5) per 1-unit increase in log-transformed (phosphorus intake), p = 0.03]. At < 1 400 mg/day, there was no association. A similar association was seen between higher phosphorus density and all-cause mortality at a phosphorus density > 0.35 mg/kcal [adjusted HR (95 % CI) 2.27 (1.19–4.33) per 0.1 mg/kcal-increase in phosphorus density, p = 0.01]. Phosphorus density was associated with cardiovascular mortality [adjusted HR (95 % CI) 3.39 (1.43–8.02) per 0.1 mg/kcal at > 0.35 mg/kcal, p = 0.01], whereas no association was shown in analyses with phosphorus intake. The Panel notes that only a single measurement, as a 24-hour dietary recall, was used to assess phosphorus intake. Moreover, the nutrient database used in this study was unable to differentiate between organic and inorganic sources of phosphorus (Anonymus, 1994).

5.4.3.1. Left ventricular mass

Yamamoto et al. (2013) investigated the association between dietary phosphorus intake and left ventricular mass in 4 494 participants from the Multi-Ethnic Study of Atherosclerosis, a community-based study of individuals free of known cardiovascular disease. The intake of dietary phosphorus was estimated using a 120-item FFQ and left ventricular mass was measured using magnetic resonance imaging. In the fully adjusted model, each 20 % higher estimated dietary phosphorus intake was associated with an estimated 1.06 g higher left ventricular mass (95 % CI 0.50–1.62, p < 0.001). The Panel notes the many limitations of this study, including its cross-sectional design.

5.4.3.2. Hypertension

Alonso et al. (2010) analysed the associations of dietary phosphorus (assessed by validated FFQ) with blood pressure at the baseline visit and incidence of hypertension in 13 444 participants from the Atherosclerosis Risk in Communities and the Multi-Ethnic Study of Atherosclerosis cohorts. They found that, compared with individuals in the lowest quintile of phosphorus intake, those in the highest quintile had lower systolic and diastolic blood pressures after adjustment for potential confounders.

Further, higher dietary phosphorus intake was associated with lower risk of development of future hypertension after adjustment for non-dietary confounders (HR 0.80 [95 % CI 0.80–1.00], comparing extreme quintiles, $p_{trend} = 0.02$), though this association was no longer significant after adjustment for dietary factors (HR 1.01 [95 % CI 0.82–1.23], $p_{trend} = 0.88$). After adjustment, only phosphorus from dairy products but not from other sources was associated with lower baseline blood pressure and reduced risk of incident hypertension. Hazard ratios (95 % CIs) comparing extreme quintiles were 0.86 (0.76–0.97, $p_{trend} = 0.01$) for phosphorus from dairy foods and 1.04 (0.93–1.17, $p_{trend} = 0.48$) for phosphorus from other foods. The Panel notes the high correlation of phosphorus with other nutrients potentially associated with blood pressure, such as calcium, magnesium, or potassium, and that the potential benefits seem to be restricted to phosphorus obtained through the intake of dairy products. This finding could be indicative of an effect of phosphorus in conjunction with other dairy constituents or of dairy foods itself, even without an involvement of phosphorus.

5.4.3.3. Conclusions on cardiovascular disease-related outcomes and all-cause mortality

The Panel considers that evidence related to all-cause mortality and cardiovascular outcomes, including blood pressure, is limited and inconsistent and cannot be used to derive DRVs for phosphorus.

6. Data on which to base Dietary Reference Values

6.1. Adults, infants aged 7–11 months and children

In the absence of suitable biomarkers of phosphorus intake or status and the fact that data on balance studies and on phosphorus intake and health outcomes cannot be used for setting DRVs for phosphorus, the Panel concludes that there are no new data to amend the basis used by the SCF (1993) for setting PRIs for phosphorus, which were derived as the equimolar relationship between calcium and phosphorus. Thus, the Panel considers to set DRVs for phosphorus in line with those for calcium (EFSA NDA Panel, 2015). This criterion for setting DRVs for phosphorus is based on the lack of consistent other evidence and takes into consideration that phosphorus and calcium are present in the body in approximately equimolar amounts (Section 2.3.7). The Panel notes that the fractional absorption of phosphorus is higher compared to calcium. However, as absorption of both minerals may vary with age and other dietary components, the Panel considers that the exact calcium-to-available phosphorus ratio cannot be determined and proposes to set DRVs for phosphorus based on the equimolar calcium-to-phosphorus ratio observed in the body.

The Panel considers that the available data are insufficient to derive ARs and PRIs for phosphorus and therefore, the Panel proposes to set AIs for all population groups. Amounts of phosphorus (in mg/day) equimolar to calcium (EFSA NDA Panel, 2015) were calculated and AIs derived after rounding down to the nearest 100 mg/day, to take into account the higher fractional absorption of phosphorus compared to calcium (Table 7).

6.2. Pregnancy and lactation

The Panel acknowledges the existence of physiological adaptive processes that ensure sufficient phosphorus for fetal growth and breast milk production. These may obviate the need in pregnancy and lactation for additional phosphorus in the diet, provided intake is close to the DRV for adults (see Section 5.3). Therefore, the Panel concludes that additional phosphorus is not required for pregnant and lactating women.

CONCLUSIONS

The Panel concludes that there are no new data to amend the basis used by the SCF (1993) for setting PRIs for phosphorus, which were derived as the equimolar relationship between calcium and phosphorus. The Panel derives AIs for phosphorus based on the PRIs proposed for calcium, in the absence of consistent other evidence. The Panel notes that the fractional absorption of phosphorus is higher compared to calcium. As absorption of both minerals may vary with age and other dietary

components, the Panel considers that the exact calcium-to-available phosphorus ratio cannot be determined and proposes to set AIs for phosphorus based on the equimolar calcium-to-phosphorus ratio, for all population groups.

Table 7: Summary of Adequate Intakes for phosphorus for infants aged 7–11 months, children and adults

Age	Adequate Intake (mg/day)
7–11 months	200
1–3 years	300
4–10 years	600
11–17 years	800
Adults ≥ 18 years [(a)]	700

(a): including pregnancy and lactation

RECOMMENDATIONS FOR RESEARCH

The Panel recommends that studies be undertaken to better characterise biomarkers of phosphorus status, including phosphatonins and especially FGF-23.

The Panel recommends research on the effect of dietary phosphorus intake on long-term health outcomes and the risk of chronic disease.

The Panel recommends the development of dietary assessment tools allowing for the quantification of phosphorus-based additives used in food processing and in some carbonated beverages.

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APPENDICES

Appendix A. Dietary surveys in the EFSA Comprehensive European Food Consumption Database included in the nutrient intake calculation and number of subjects in the different age classes

Country	Dietary survey (year)	Year	Method	Days	Age (years)	Number of subjects [b]						
						Infants 1-11 mo	Children 1–< 3 y	Children 3–< 10 y	Children 10–< 18 y	Adults 18–< 65 y	Adults 65–< 75 y	Adults ≥ 75 y
Finland/1	DIPP	2000–2010	Dietary record	3	0.5–6	499	500	750				
Finland/2	NWSSP	2007–2008	48-hour dietary recall [a]	2 × 2 [a]	13–15				306			
Finland/3	FINDIET2012	2012	48-hour dietary recall [a]	2 [a]	25–74					1 295	413	
France	INCA2	2006–2007	Dietary record	7	3–79			482	973	2 276	264	84
Germany/1	EsKiMo	2006	Dietary record	3	6–11			835	393			
Germany/2	VELS	2001–2002	Dietary record	6	<1–4	158	347	299				
Ireland	NANS	2008–2010	Dietary record	4	18–90					1 274	149	77
Italy	INRAN-SCAI 2005-06	2005–2006	Dietary record	3	<1–98	16 [b]	36 [b]	193	247	2 313	290	228
Latvia	FC_PREGNANTWOMEN 2011	2011	24-hour dietary recall	2	15–45				12 [b]	991 [c]		
Netherlands	DNFCS	2007–2010	24-hour dietary recall	2	7–69			447	1 142	2 057	173	
Sweden	RISKMATEN	2010–2011	Dietary records (Web)	4	18–80					1 430	295	72
UK/1	DNSIYC	2011	Dietary record	4	0.3–1.5	1 369	1 314					
UK/2	NDNS-Rolling Programme (1–3 y)	2008–2011	Dietary record	4	1-94		185	651	666	1 266	166	139

mo, months; y, years; DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale de Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione - Studio sui Consumi Alimentari in Italia; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a): A 48-hour dietary recall comprises two consecutive days.

(b): 5^{th} or 95^{th} percentile intakes calculated from fewer than 60 subjects require cautious interpretation as the results may not be statistically robust (EFSA, 2011b) and, therefore, for these dietary surveys/age classes, the 5^{th} and 95^{th} percentile estimates will not be presented in the intake results.

(c): One subject with only one 24-hour dietary recall day was excluded from the dataset, i.e. final n = 990.

Appendix B. Phosphorus intakes in males in different surveys according to age classes and country

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n [(a)]	Average	Median	P5	P95	n	Average	Median	P5	P95
< 1 year [(b)]	Finland	DIPP_2001_2009	247	273	283	32	528	245	140	136	89	202
	Germany	VELS	84	431	400	245	694	84	132	127	82	190
	Italy	INRAN_SCAI_2005_06	9	326	207	[(c)]	[(c)]	9	102	106	[(c)]	[(c)]
	United Kingdom	DNSIYC_2011	699	531	511	244	879	699	154	151	93	227
1 to < 3 years	Finland	DIPP_2001_2009	245	719	669	337	1213	245	196	192	113	290
	Germany	VELS	174	699	682	396	1018	174	149	146	94	204
	Italy	INRAN_SCAI_2005_06	20	924	924	[(c)]	[(c)]	20	189	186	[(c)]	[(c)]
	United Kingdom	DNSIYC_2011	663	871	851	439	1310	663	207	207	127	290
	United Kingdom	NDNS-RollingProgrammeYears1-3	107	973	974	570	1461	107	198	201	130	262
3 to < 10 years	Finland	DIPP_2001_2009	381	1173	1176	695	1633	381	200	202	135	259
	France	INCA2	239	1033	1000	618	1468	239	167	161	117	241
	Germany	EsKiMo	426	1151	1126	751	1645	426	151	149	110	192
	Germany	VELS	146	808	767	512	1201	146	144	139	106	201
	Italy	INRAN_SCAI_2005_06	94	1202	1144	812	1734	94	165	160	122	225
	Netherlands	DNFCS 2007-2010	231	1146	1107	689	1700	231	133	133	86	184
	United Kingdom	NDNS-RollingProgrammeYears1-3	326	1076	1052	673	1558	326	171	168	121	240
10 to < 18 years	Finland	NWSSP07_08	136	1601	1537	980	2459	136	196	190	126	275
	France	INCA2	449	1243	1210	745	1828	449	159	155	116	213
	Germany	EsKiMo	197	1225	1169	792	1826	197	151	148	107	204
	Italy	INRAN_SCAI_2005_06	108	1494	1405	944	2244	108	152	148	123	193
	Netherlands	DNFCS 2007-2010	566	1397	1334	791	2207	566	131	128	84	189
	United Kingdom	NDNS-RollingProgrammeYears1-3	340	1231	1187	726	1845	340	151	149	110	206
18 to < 65 years	Finland	FINDIET2012	585	1614	1548	793	2640	585	174	172	117	242
	France	INCA2	936	1403	1372	801	2103	936	161	158	120	212
	Ireland	NANS_2012	634	1767	1745	985	2702	634	177	175	125	241
	Italy	INRAN_SCAI_2005_06	1068	1378	1334	820	2089	1068	151	148	119	192
	Netherlands	DNFCS 2007-2010	1023	1671	1628	961	2520	1023	149	146	100	211
	Sweden	Riksmaten 2010	623	1692	1651	961	2583	623	173	172	127	227
	United Kingdom	NDNS-RollingProgrammeYears1-3	560	1448	1411	810	2223	560	166	163	115	228

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n [(a)]	Average	Median	P5	P95	n	Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	210	1426	1367	665	2251	210	175	171	120	245
	France	INCA2	111	1372	1351	787	1931	111	161	158	124	211
	Ireland	NANS_2012	72	1652	1638	854	2683	72	189	189	133	265
	Italy	INRAN_SCAI_2005_06	133	1311	1315	791	1945	133	150	149	117	193
	Netherlands	DNFCS 2007-2010	91	1478	1448	717	2233	91	162	163	111	213
	Sweden	Riksmaten 2010	127	1558	1528	981	2250	127	182	176	142	233
	United Kingdom	NDNS-RollingProgrammeYears1-3	75	1498	1479	607	2341	75	180	175	122	245
≥ 75 years	France	INCA2	40	1280	1173	(c)	(c)	40	165	162	(c)	(c)
	Ireland	NANS_2012	34	1484	1402	(c)	(c)	34	193	191	(c)	(c)
	Italy	INRAN_SCAI_2005_06	69	1332	1279	828	1941	69	153	152	121	190
	Sweden	Riksmaten 2010	42	1531	1637	(c)	(c)	42	182	181	(c)	(c)
	United Kingdom	NDNS-RollingProgrammeYears1-3	56	1253	1169	(c)	(c)	56	175	177	(c)	(c)

P5, 5th percentile; P95, 95th percentile; DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale de Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a): Number of individuals in the population group.

(b): The proportions of breast-fed infants were 58 % in the Finnish survey, 40 % in the German survey, 44 % in the Italian survey, and 21 % in the UK survey. Most infants were partially breast-fed. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different age. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. As no information on the breastfeeding events were reported in the Finnish survey, breast milk intake was not taken into consideration in the intake estimates of Finnish infants.

(c): 5th or 95th percentile intakes calculated from fewer than 60 subjects require cautious interpretation as the results may not be statistically robust (EFSA, 2011b) and, therefore, for these dietary surveys/age classes, the 5th and 95th percentile estimates will not be presented in the intake results.

Appendix C. Phosphorus intakes in females in different surveys according to age classes and country

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n [(a)]	Average	Median	P5	P95	n	Average	Median	P5	P95
< 1 year [(b)]	Finland	DIPP_2001_2009	253	265	264	32	533	251	151	146	93	220
	Germany	VELS	75	368	354	203 [(c)]	604 [(c)]	75	125	128	80 [(c)]	173 [(c)]
	Italy	INRAN_SCAI_2005_06	7	447	509			7	145	151		
	United Kingdom	DNSIYC_2011	670	480	448	216	857	670	154	150	78	244
1 to < 3 years	Finland	DIPP_2001_2009	255	711	706	295	1164	255	206	203	116	299
	Germany	VELS	174	641	645	357 [(c)]	932 [(c)]	174	149	146	102 [(c)]	207 [(c)]
	Italy	INRAN_SCAI_2005_06	16	890	846			16	196	189		
	United Kingdom	DNSIYC_2011	651	815	802	419	1266	651	205	208	123	285
	United Kingdom	NDNS-RollingProgrammeYears1-3	78	863	856	499	1224	78	192	190	132	254
3 to < 10 years	Finland	DIPP_2001_2009	369	1086	1068	699	1551	369	206	206	149	269
	France	INCA2	243	925	901	625	1274	243	167	162	122	228
	Germany	EsKiMo	409	1056	1032	667	1536	409	156	155	113	200
	Germany	VELS	147	750	742	483	1076	147	145	142	103	200
	Italy	INRAN_SCAI_2005_06	99	1155	1138	694	1672	99	160	156	120	226
	Netherlands	DNFCS 2007-2010	216	1080	1033	642	1693	216	133	132	84	192
	United Kingdom	NDNS-RollingProgrammeYears1-3	325	991	980	587	1458	325	166	165	120	222
10 to < 18 years	Finland	NWSSP07_08	170	1264	1255	691	2045	170	192	192	127	255
	France	INCA2	524	992	983	574	1460	524	158	153	115	214
	Germany	EsKiMo	196	1148	1130	729	1633	196	155	151	110	207
	Italy	INRAN_SCAI_2005_06	139	1226	1217	813 [(c)]	1836 [(c)]	139	154	152	117 [(c)]	205 [(c)]
	Latvia [(d)]	FC_PREGNANTWOMEN_2011	12	1561	1458			12	155	152		
	Netherlands	DNFCS 2007-2010	576	1167	1138	674	1716	576	133	134	82	189
	United Kingdom	NDNS-RollingProgrammeYears1-3	326	990	977	573	1525	326	147	143	105	205
18 to < 65 years	Finland	FINDIET2012	710	1293	1242	706	2057	710	181	176	117	264
	France	INCA2	1340	1084	1060	619	1612	1340	169	163	122	235
	Ireland	NANS_2012	640	1302	1274	750	1964	640	178	173	127	241
	Italy	INRAN_SCAI_2005_06	1245	1151	1124	687	1685	1245	157	154	120	206
	Latvia [(d)]	FC_PREGNANTWOMEN_2011	990	1541	1443	892	2568	990	182	167	114	299
	Netherlands	DNFCS 2007-2010	1034	1279	1241	729	1967	1034	155	151	100	228
	Sweden	Riksmaten 2010	807	1336	1301	800	1989	807	184	173	128	238
	United Kingdom	NDNS-RollingProgrammeYears1-3	706	1127	1106	627	1701	706	171	167	116	240

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n [(a)]	Average	Median	P5	P95	n	Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	203	1153	1140	644	1690	203	187	187	124	258
	France	INCA2	153	1050	1034	557	1487	153	170	163	127	233
	Ireland	NANS_2012	77	1372	1333	819	2069	77	202	198	145	261
	Italy	INRAN_SCAI_2005_06	157	1098	1082	631	1643	157	159	155	114	219
	Netherlands	DNFCS 2007-2010	82	1181	1148	640	1720	82	163	159	111	237
	Sweden	Riksmaten 2010	168	1310	1272	781	1972	168	188	188	148	237
	United Kingdom	NDNS-RollingProgrammeYears1-3	91	1145	1144	714	1618	91	191	185	139	264
≥ 75 years	France	INCA2	44	1000	975	[(c)]	[(c)]	44	167	164	[(c)]	[(c)]
	Ireland	NANS_2012	43	1294	1275	[(c)]	[(c)]	43	207	200	[(c)]	[(c)]
	Italy	INRAN_SCAI_2005_06	159	1075	1080	623	1490	159	161	155	117	218
	Sweden	Riksmaten 2010	30	1330	1316	[(c)]	[(c)]	30	189	189	[(c)]	[(c)]
	United Kingdom	NDNS-RollingProgrammeYears1-3	83	1162	1139	728	1596	83	193	194	140	249

P5, 5th percentile; P95, 95th percentile; DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale de Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a): Number of individuals in the population group.

(b): The proportions of breast-fed infants were 58 % in the Finnish survey, 40 % in the German survey, 44 % in the Italian survey, and 21 % in the UK survey. Most infants were partially breast-fed. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different age. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. As no information on the breastfeeding events were reported in the Finnish survey, breast milk intake was not taken into consideration in the intake estimates of Finnish infants.

(c): 5th or 95th percentile intakes calculated from fewer than 60 subjects require cautious interpretation as the results may not be statistically robust (EFSA, 2011b) and, therefore, for these dietary surveys/age classes, the 5th and 95th percentile estimates will not be presented in the intake results.

(d): Pregnant women only.

Appendix D. Minimum and maximum % contribution of different food groups to phosphorus intakes in males

Food groups	Age (years)						
	< 1	1 to < 3	3 to < 10	10 to < 18	18 to < 65	65 to < 75	≥ 75
Additives, flavours, baking and processing aids	<1	<1	0–1	0–1	0	0	0
Alcoholic beverages	<1	<1	<1	<1–1	2–5	1–4	1–3
Animal and vegetable fats and oils	<1	<1	<1–1	<1	<1–1	<1–1	<1–1
Coffee, cocoa, tea and infusions	<1	<1–1	<1–2	1–2	1–6	1–6	1–7
Composite dishes	<1–3	<1–8	<1–9	<1–13	<1–12	1–10	<1–10
Eggs and egg products	<1–1	1–2	1–4	1–4	1–4	1–4	1–3
Fish, seafood, amphibians, reptiles and invertebrates	<1–1	1–6	1–5	1–6	2–7	3–9	5–9
Food products for young population	26–50	2–8	<1–1	<1	<1	–	–
Fruit and fruit products	1–6	2–3	1–2	1–2	1–2	1–3	1–3
Fruit and vegetable juices and nectars	<1–1	<1–1	1–2	1–2	<1–1	<1–1	<1–1
Grains and grain-based products	4–16	18–27	16–33	19–34	20–29	20–33	21–35
Human milk	<1–16	<1	–	–	–	–	–
Legumes, nuts, oilseeds and spices	<1–2	1–3	1–4	1–3	2–4	1–4	1–3
Meat and meat products	1–9	5–11	9–19	12–23	14–25	12–23	11–21
Milk and dairy products	17–29	42–48	32–52	23–47	19–35	18–35	20–30
Products for non-standard diets, food imitates and food supplements or fortifying agents	0–1	0–1	0–1	<1	<1–1	<1–1	0–1
Seasoning, sauces and condiments	<1–1	<1–1	<1–1	<1–1	<1–1	<1–1	<1–1
Starchy roots or tubers and products thereof, sugar plants	<1–6	1–5	2–6	2–7	2–6	2–5	3–5
Sugar, confectionery and water-based sweet desserts	<1	<1–3	1–5	1–5	<1–1	<1–1	<1–1
Vegetables and vegetable products	1–7	2–3	2–4	2–5	2–6	2–6	2–6
Water and water-based beverages	<1	<1–1	<1–2	1–4	<1–3	<1–1	<1

"–" means that there was no consumption event of the food group for the age and sex group considered, whereas "0" means that there were some consumption events, but that the food group does not contribute to the intake of the nutrient considered, for the age and sex group considered.

Appendix E. Minimum and maximum % contribution of different food groups to phosphorus intakes in females

Food groups	Age (years)						
	< 1	1 to < 3	3 to < 10	10 to < 18	18 to < 65	65 to < 75	≥ 75
Additives, flavours, baking and processing aids	<1	0	0–1	0–1	0	<1	0
Alcoholic beverages	<1	<1	<1	<1	<1–2	<1–1	<1–1
Animal and vegetable fats and oils	<1	<1	<1–1	<1–1	<1–1	<1–1	<1–1
Coffee, cocoa, tea and infusions	<1–3	<1–5	<1–2	<1–2	1–7	1–7	1–7
Composite dishes	<1–3	<1–7	<1–9	<1–13	1–12	<1–9	<1–10
Eggs and egg products	<1–1	1–2	1–4	1–4	1–3	1–3	1–4
Fish, seafood, amphibians, reptiles and invertebrates	<1–2	1–7	<1–5	1–7	2–7	3–9	3–8
Food products for young population	23–60	2–9	<1	<1	<1	–	<1
Fruit and fruit products	2–5	2–3	1–2	1–3	1–3	2–4	2–4
Fruit and vegetable juices and nectars	<1–1	<1–1	1–2	1–2	<1–1	<1–1	<1–1
Grains and grain-based products	10–16	17–28	17–33	21–33	19–38	18–32	17–33
Human milk	<1–6	<1	–	–	–	–	–
Legumes, nuts, oilseeds and spices	<1–3	1–3	1–4	1–3	2–4	2–4	2–3
Meat and meat products	1–8	5–10	8–19	11–22	12–21	12–20	10–19
Milk and dairy products	10–38	40–52	32–53	22–45	21–39	23–36	23–33
Products for non-standard diets, food imitates and food supplements or fortifying agents	0	0–1	0–1	<1–1	<1–2	<1–1	0–2
Seasoning, sauces and condiments	<1	<1–1	<1–1	<1–1	<1–1	<1–1	<1–1
Starchy roots or tubers and products thereof, sugar plants	1–6	2–4	2–6	2–8	2–6	2–5	2–4
Sugar, confectionery and water-based sweet desserts	<1–1	<1–2	1–5	1–5	<1–2	<1–1	<1–1
Vegetables and vegetable products	2–7	2–3	2–4	3–5	2–7	2–7	2–6
Water and water-based beverages	<1	<1–1	<1–2	<1–3	<1–2	<1	<1

"–" means that there was no consumption event of the food group for the age and sex group considered, whereas "0" means that there were some consumption events, but that the food group does not contribute to the intake of the nutrient considered, for the age and sex group considered.

1785 **ABBREVIATIONS**

$1,25(OH)_2D_3$	1,25-dihydroxy-vitamin D (calcitriol, the active metabolite of vitamin D)
Afssa	Agence française de sécurité sanitaire des aliments
AI	Adequate Intake
AR	Average Requirement
ATBC	Alpha-Tocopherol Beta-Carotene Cancer Prevention
ATP	adenosine triphosphate
BMD	bone mineral density
BMC	bone mineral content
cAMP	cyclic adenosine monophosphate
cGMP	cyclic guanine monophosphate
COMA	Committee on Medical Aspects of Food Policy
CI	confidence interval
CVD	cardiovascular disease
D-A-CH	Deutschland–Austria–Confoederatio Helvetica
DH	UK Department of Health
DIPP	type 1 Diabetes Prediction and Prevention survey
DNFCS	Dutch National Food Consumption Survey
DNSIYC	Diet and Nutrition Survey of Infants and Young Children
DRV	Dietary Reference Value
DXA	dual-energy X-ray absorptiometry
EAR	Estimated Average Requirement
EsKiMo	Ernährungsstudie als KIGGS-Modul
FAO	Food and Agriculture Organization of the United Nations
FC_PREGNANTWOMEN	food consumption of pregnant women in Latvia
FFQ	food frequency questionnaire
FGF-23	fibroblast growth factor-23

FINDIET	the national dietary survey of Finland
HR	hazard ratio
INCA	étude Individuelle Nationale de Consommations Alimentaires
INRAN-SCAI	Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia
IOM	US Institute of Medicine of the National Academy of Sciences
NaPi-IIa, NaPi-IIb, NaPi-IIc	sodium-dependent phosphate transporters
NANS	National Adult Nutrition Survey
NDNS	UK National Diet and Nutrition Survey
NHANES	National Health and Nutrition Examination Survey
NNR	Nordic Nutrition Recommendations
NWSSP	Nutrition and Wellbeing of Secondary School Pupils
PRI	Population Reference Intake
PTH	parathyroid hormone
RDA	Recommended Dietary Allowance
RNI	Reference Nutrient Intake
RR	relative risk
SCF	Scientific Committee for Food
SD	standard deviation
SU.VI.MAX	SUpplémentation en VItamines et Minéraux Anti-oXydants
VELS	Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln
WHO	World Health Organization

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