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SCIENTIFIC OPINION

Scientific Opinion on Dietary Reference Values for phosphorus¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies derived Dietary Reference Values (DRVs) for phosphorus. The Panel considered data from balance studies, losses of phosphorus from the body and intestinal absorption for possible use in a factorial approach, and studies on phosphorus intake and long-term health outcomes. The Panel concluded that these data were insufficient for setting DRVs for phosphorus. Data on the calcium to phosphorus ratio in bones of healthy adults, adjusted for the proportion of phosphorus found outside bone, and data on whole-body calcium and phosphorus contents in Caucasian adults indicate that the calcium to phosphorus molar ratio in the body ranges from 1.4:1 to 1.9:1. Although the fractional absorption of phosphorus is higher than that of calcium, the Panel considered that the actual amounts of calcium and phosphorus that are available for absorption from the diet cannot be determined; therefore, the whole-body calcium to phosphorus ratio was used to set DRVs. The data were considered insufficient to derive Average Requirements and Population Reference Intakes. Based on the DRVs for calcium and considering a molar calcium to phosphorus ratio of 1.4:1 to 1.9:1, amounts of phosphorus were calculated. The Panel chose the lower bound of this range (a ratio of 1.4:1, which results in a higher phosphorus intake value) for setting an Adequate Intake (AI), taking into account estimated phosphorus intakes in Western countries, which are considerably higher than the values calculated. The AI is 160 mg/day for infants (7–11 months) and between 250 and 640 mg/day for children. For adults, the AI is 550 mg/day. 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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KEY WORDS

phosphorus, calcium, molar ratio, 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 (DRVs) for the European population, including phosphorus.

Phosphorus is involved in many physiological processes, such as in the cell's energy cycle, in 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 bones and teeth, 14 % is in soft tissues, including muscle, liver, heart and kidney, 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), 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, limited data suggest that net phosphorus absorption ranges from 55 to 80 % of intake. Phosphorus absorption is affected by the total amount of phosphorus in the diet and also by the type of phosphorus (organic versus inorganic), the food origin (animal-versus plant-derived) and the ratio of phosphorus to other dietary components. Absorption is regulated by 1,25(OH)₂D and PTH.

Hypophosphataemia, defined by a serum inorganic phosphorus concentration of < 0.80 mmol/L (2.48 mg/dL), only rarely occurs because of inadequate dietary phosphorus intake, and is generally 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 13 dietary surveys in nine European Union countries, mean phosphorus intakes range from 265 to 531 mg/day in infants, from 641 to 973 mg/day in children aged 1 to < 3 years, from 750 to 1 202 mg/day in children aged 3 to < 10 years, from 990 to 1 601 mg/day in children aged 10 to < 18 years and from 1 000 to 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. In addition, it was considered that estimations of phosphorus absorption from the diet, as well as losses of phosphorus via urine and faeces, vary over a wide range, so that the factorial approach cannot be used for deriving the requirement 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.

Data on the molar ratio of calcium to phosphorus in intact bone of healthy adults suggest a range of approximately 1.6:1 to 1.8:1. Using the calcium to phosphorus molar ratio in bone of 1.6:1 to 1.8:1 and adjusting for the proportion of calcium and phosphorus found outside bone, a molar ratio of calcium to phosphorus in the adult body of about 1.37:1 to 1.55:1 is estimated. In addition, data from measurements of whole-body calcium and phosphorus contents in Caucasian men and women indicate that the calcium to phosphorus molar ratio in the whole body ranges from 1.48:1 to 1.69:1 in women and from 1.57:1 to 1.89:1 in men. The Panel thus considered that the ratio of calcium to phosphorus in the whole body ranges from about 1.4:1 to 1.9:1 and proposed, in the absence of other consistent evidence, that DRVs for phosphorus be set based on the approximate molar ratio of calcium to phosphorus in the body. The fractional absorption of phosphorus is higher than that of calcium. However, as phosphorus absorption has been reported to vary over a wide range, it was considered that the actual amounts of calcium to phosphorus that are available for absorption from the diet and

that may be retained in the body cannot be determined. In the absence of this information, the Panel proposed to set DRVs for phosphorus based solely on the range of the molar ratio of calcium to phosphorus in the whole body. The Panel considered that the data are insufficient to derive Average Requirements and Population Reference Intakes (PRIs) for phosphorus and proposed to set Adequate Intakes (AIs) for all population groups. Based on the AI (for infants aged 7–11 months) and the PRIs (for all other ages) for calcium and considering a molar calcium to phosphorus ratio of 1.4:1 to 1.9:1, adequate quantities of phosphorus were calculated in mg/day. The Panel chose the lower bound of this range (i.e. a ratio of 1.4:1 which results in the higher phosphorus intake value) for setting an AI for phosphorus, taking into account estimated phosphorus intakes in Western countries which are considerably higher than the calculated values.

The AI is 160 mg/day for infants aged 7–11 months and between 250 mg/day and 640 mg/day for children. For adults, the AI is 550 mg/day. Taking into consideration adaptive changes in phosphorus metabolism that may 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;
- Fats, including saturated fatty acids, polyunsaturated fatty acids and monounsaturated fatty acids, *trans* fatty acids;

⁴ Scientific Committee for Food, 1993. Nutrient and energy intakes for the European Community. Reports of the Scientific Committee for Food, 31st series. Food – Science and Technique, European Commission, Luxembourg, 248 pp.

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.

- 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 in the cell's energy cycle, in 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 6 months of age, for children and for pregnant and lactating women.

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 abundant element in the earth's crust. It is a non-metal, solid chemical element and belongs to Group 15 (VA) of the periodic table of the elements. It has the atomic number 15 and an atomic mass of 30.97 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 because of its high reactivity, but is found in the form of phosphate minerals. The most abundant form is apatite (and related minerals), i.e. hydroxyapatite ($\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6$), chlorapatite ($\text{Ca}_{10}\text{Cl}_2(\text{PO}_4)_6$) and fluorapatite ($\text{Ca}_{10}\text{F}_2(\text{PO}_4)_6$). There is only one stable phosphorus isotope, that is ^{31}P . There are, however, several 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 bones and teeth, in the form of hydroxyapatite, and together phosphorus and calcium account for around 80–90 % of bone composition. Hydroxyapatite forms the mineralised 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 ($1,25(\text{OH})_2\text{D}$), 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 sugars, proteins and enzymes in the body are phosphorylated, and that process often determines the activity and function of sugars and phosphoproteins. Phosphorus is an integral component of adenosine triphosphate (ATP), the body's key energy source. Other phosphorylated molecules (e.g. creatine phosphate in muscle) serve as a

rapid source of phosphate for ATP production and energy transduction in substrate metabolism. Many intracellular signalling processes depend on phosphorus-containing compounds such as cyclic adenosine monophosphate (cAMP), cyclic guanosine monophosphate (cGMP) and inositol polyphosphates (e.g. inositol triphosphate (IP₃)). Phosphorus, as 2,3-bisphosphoglycerate (also termed 2,3-diphosphoglycerate), plays an important role in the dissociation of oxygen from haemoglobin. Cellular phosphate is the main intracellular buffer and therefore is essential for pH regulation in the human body (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 concentrations below 0.80 mmol/L (2.48 mg/dL) in adults. This occurs only rarely 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 sub-groups of patients, such as those with sepsis, chronic alcoholism, major trauma or chronic obstructive pulmonary disease (Gaasbeek and Meinders, 2005; Brunelli and Goldfarb, 2007). Hypophosphataemia may also occur during the management of diabetic ketoacidosis because the administration of insulin drives glucose and phosphorus into cells and causes a rapid fall in serum phosphate concentrations. Mild hypophosphataemia can also occur as a common, generally asymptomatic, consequence of hyperparathyroidism (O'Brien et al., 2014).

The clinical symptoms of hypophosphataemia usually occur when serum phosphorus concentrations fall below 0.3 mmol/L (\approx 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, depending on 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, paraesthesia, ataxia, confusion and even death. The muscle weakness involves, in particular, 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 and form growth plate cartilage and bone matrix, together with the 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 plate 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 of 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.

Gastro-intestinal 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 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, net phosphorus absorption typically ranges from 55 to 80 % of customary intakes, and in infants from 65 to 90 % (Heaney, 2012; O'Brien et al., 2014). Intestinal phosphorus absorption tends to decrease with ageing. Within the gut lumen, phosphatases hydrolyse the organic forms to release inorganic phosphate. Inorganic phosphate is absorbed along the entire intestine, with most being absorbed by the small intestine (Sabbagh et al., 2011). Dietary phosphorus, 1,25(OH)₂D 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 (sFRP-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), that are also expressed in the renal tubule; however, it is NaPi-IIb that 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 to 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 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 or not 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 of phosphorus (organic versus inorganic), the food origin (animal- versus plant-derived) and the 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. In addition, 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 absorption is co-ingested calcium, which binds phosphorus in the digestive chyme, thereby preventing its absorption (Heaney, 2012; O'Brien et al., 2014). In two human metabolic balance studies with a total of 566 measurements from 284 subjects, Heaney and Nordin (2002) showed that calcium intake is the main dietary determinant of phosphorus absorption. Based on 470 measurements from 191 women, the authors estimated that each

increase in calcium intake of 0.5 g (12.5 mmol) decreases phosphorus absorption by 0.166 g (5.4 mmol). Phosphorus originating from food additives, i.e. already in an ionised inorganic form, is absorbed more readily than organic phosphorus naturally occurring in animal and plant foods (Kalantar-Zadeh et al., 2010).

The Panel notes that phosphorus absorption from the diet has been reported to vary over a wide range.

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, the 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 concentration of phosphate in human serum/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. Serum phosphorus concentration fluctuates with age (it is higher in children than in adults), acid–base status and dietary intake (Marks et al., 2010) (see Section 2.4.1.1). The increased serum phosphorus concentration following ingestion of phosphorus then depresses the serum calcium ion (Ca^{2+}) 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 required 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 early 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 bones and teeth, with the remainder distributed among other tissues (14 %) and extracellular fluid (1 %) (O'Brien et al., 2014). Thus, like calcium (although more pronounced), serum measurements reflect only 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 and rely on supplies from 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 phosphorus (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 towards adult values, consistent with resolution of transient hypoparathyroidism in the newborn (Kovacs, 2014).

2.3.3.1. Ratio of calcium to phosphorus in the bone and whole body

Calcium and phosphorus are both required for bone mineral deposition and maintenance throughout life. The calcium to phosphorus ratio in bone has been measured using instrumental neutron activation analysis. Measurement of intact bone of 37 females and 45 males aged 15–55 years showed a mean calcium to phosphorus mass ratio of 2.33:1 ± 0.34:1 (range 2.05:1 to 2.62:1) in rib bone (Tzaphlidou and Zaichick, 2002), 2.17:1 ± 0.31:1 in cortical bone (Zaichick and Tzaphlidou, 2002) and 2.07:1 ± 0.23:1 (range 1.55:1 to 2.72:1) in trabecular bone of the femoral neck (Zaichick and Tzaphlidou, 2003). These mean mass ratios of calcium to phosphorus measured in different skeletal sites are equivalent to mean molar ratios of 1.6:1 to 1.8:1 in the bone of healthy adolescents and adults.

The Panel notes that, while the majority (99 %) of body calcium is in bone (EFSA NDA Panel, 2015), about 15 % of body phosphorus is outside bone as a key functional component in other tissues (14 %) and extracellular fluid (1 %) (Section 2.3.3). Thus, using the calcium to phosphorus molar ratio in bone of 1.6:1 to 1.8:1 and adjusting for the amount of phosphorus outside bone, a molar ratio of calcium to phosphorus in the adult body of about 1.37:1 to 1.55:1 (1.6:1 divided by 0.99:0.85 to 1.8:1 divided by 0.99:0.85) may be estimated.

Outside the skeleton, phosphorus and calcium have essential and distinct physiological functions which are mediated independently and separately by specific transporters, the precise regulation of which, in the case of phosphorus, has not been fully elucidated.

Using total body neutron activation analysis, Ellis (1990) measured whole-body contents of calcium and phosphorus in 1 134 Caucasian women aged between 20 and 74 years and in 175 Caucasian men aged between 20 and 90 years in the USA. From these, mass ratios may be calculated that range from 1.92:1 to 2.18:1 according to age in women, and from 2.04:1 to 2.44:1 in men. These mass ratios are equivalent to molar ratios of calcium to phosphorus in the whole body of 1.48:1 to 1.69:1 in women and 1.57:1 to 1.89:1 in men.

Taking into account the molar calcium to phosphorus ratio in the whole body estimated from the molar ratio of calcium to phosphorus in bone and the observations of Ellis (1990), the Panel considers that the ratio of calcium to phosphorus in the whole body ranges from about 1.4:1 to 1.9:1. The Panel notes the absence of specific data for infants and children up to 15 years of age.

2.3.4. Storage

Total body phosphorus in adults has been reported to be in the order of 400–800 g, and most of this is located in the bones and teeth (Moe, 2008). Using total body neutron activation analysis, total body phosphorus (mean ± standard deviation (SD)) ranged from 374 ± 60 g to 439 ± 70 g in 1 134 Caucasian women aged between 20 and 74 years and from 461 ± 82 g to 561 ± 69 g in 175 Caucasian men aged between 20 and 90 years in the USA (Ellis, 1990).

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 8 weeks of pregnancy (Widdowson and Spray, 1951). Assuming continuous growth and maturity at 18 years, it has been estimated that continuous 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, while at age 4–12 months, accretion rates of 66 mg/day have been estimated (Prentice and Bates, 1994).

2.3.5. Metabolism

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) and the phosphatonin fibroblast growth factor-23 (FGF-23), mainly produced and secreted by osteocytes in bone (Berndt and Kumar, 2009; Bergwitz and Jüppner, 2010). An elevation in serum phosphorus concentration as a result of a diet high in phosphorus leads to a decrease in serum calcium concentration and an increase in PTH release resulting in increased renal phosphate excretion. The increase in serum inorganic phosphate additionally results in a reduced 1,25(OH)₂D synthesis which in turn leads to a reduced intestinal phosphorus absorption (Berndt and Kumar, 2009; Bergwitz and Jüppner, 2010). An increase in serum phosphorus concentration 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 concentration, with a subsequent decrease in intestinal phosphorus absorption (Quarles, 2008). On the other hand, a decrease in serum phosphorus concentration as a result of a diet low in phosphorus leads to an increase in serum calcium concentration and a decrease in PTH release resulting in decreased renal phosphorus excretion. Additionally, a decrease in serum phosphorus concentration leads to an increased 1,25(OH)₂D synthesis and subsequent enhanced phosphorus absorption by the intestine (Berndt and Kumar, 2009; Bergwitz and Jüppner, 2010). Finally, a decrease in serum phosphorus concentration 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 to be 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 numbers 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, 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 sFRP-4 (Schiavi and Kumar, 2004; Berndt and Kumar, 2009). FGF-23, along with PTH, regulates 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 the regulation of renal phosphorus handling (Hu et al., 2010). Phosphatonins, and in particular FGF-23, and *klotho* are also postulated to be involved in phosphorus homeostasis in pathophysiological conditions associated with phosphorus wasting.

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 to 600 mg/day (Greger et al., 1978; Anderson, 2005; Delgado-Andrade et al., 2011). Total faecal phosphorus, however, represents both non-absorbed phosphorus from food, and losses of endogenous phosphorus. The latter are mainly derived from digestive secretions that have not been reabsorbed. The daily faecal loss of endogenous phosphorus is 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 route of phosphorus loss. 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. Atkinson et al. (1995) reported an average phosphorus concentration in human milk of about 160 mg/L at 14 days, 140 mg/L at 30 and 90 days and 120 mg/L at 180 days post partum.

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 \pm SD) 172 \pm 23 mg/L in 60 women in Sweden after 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 after 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 after 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 the phosphorus concentration of breast milk from mothers of term infants were available from seven studies, and these results are summarised in Table 1 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

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).
n, number of samples.

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 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 regarding 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. This 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 Dietary Reference Value (DRV) for adults.

2.3.7. Interaction with other nutrients

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 because of 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/plasma phosphorus concentration

Serum/plasma inorganic phosphorus has been proposed as an indicator of adequacy of phosphorus intake (IOM, 1997), mainly based on the equation proposed by Nordin (1989), derived from data from an infusion study (Bijovet, 1969). This equation was established in adults with normal renal function who were infused with < 20 mmol/day (< 619 mg/day) of phosphorus. The relationship became weaker at higher amounts of infused phosphorus. Since serum phosphorus concentration is maintained within a relatively narrow range by different homeostatic mechanisms (Section 2.3.5), the effect of dietary phosphorus intake on serum phosphorus concentration 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 concentration in fasting and non-fasting samples from 15 513 participants has been evaluated using data from 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 increment in phosphorus intake 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 (25th–75th percentile intake in men and women, 952–1 511 mg/day and 826–1 315 mg/day, respectively) and serum phosphorus concentration (Mataix et al., 2006). A possible explanation for these weak and inconsistent findings is that the renal clearance of plasma phosphorus is so finely regulated that fasting serum/plasma phosphorus concentration shows only minimal changes even in the presence of wide variations in intake. In most observational studies, serum phosphorus concentration was measured in only 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 concentration throughout the day and subsequently averaging 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 phosphorus concentration, compared with the concentration measured during 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 phosphorus concentration was observed during phosphorus loading (3 000 mg/day for 10 days). Fasting serum phosphorus concentrations were unmodified during both restriction and loading periods compared with the control period (Portale et al., 1987).

The Panel notes that serum phosphorus concentration cannot be considered 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 as a result of homeostatic mechanisms. Moreover, because of fine renal regulation, fasting serum phosphorus concentration shows 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/plasma 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/plasma 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 biomarker as its concentration is affected by vitamin D status as well as serum ionised calcium and phosphorus concentrations.

2.4.2.4. Other biomarkers

In addition to PTH, other phosphorus-regulating factors, such as FGF-23 and klotho, a protein present both in membranes and in circulation and needed for FGF-23 to bind to its receptor, have recently been suggested as possible biomarkers of phosphorus status (see Gutierrez (2013)). However, the Panel considers that there is as yet insufficient information to conclude on the use of these factors as biomarkers of phosphorus status.

2.4.2.5. Conclusions on biomarkers of phosphorus intake and status

The Panel considers that there is currently no reliable biomarker of phosphorus intake and status that may be used for deriving the requirement for phosphorus.

2.5. Effects of genotypes

The understanding of phosphorus homeostasis has largely been obtained from molecular studies of human inherited genetic disorders (Bergwitz and Jüppner, 2010) 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 encoding phosphate transporters NPT2 and PiT 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 (*PHEX*) with homology to endopeptidases on the X-chromosome (Tenenhouse, 2005).

The Panel notes that, although genetic defects leading to a number of rare disorders affecting phosphorus homeostasis have been characterised at the molecular level, no genotypes have been identified that would require consideration with regard to 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, i.e. milk and milk products 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 foods⁶ 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.⁷ The phosphorus content of infant and follow-on formulae⁸ 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 are likely to underestimate the contribution from phosphate-containing additives (Oenning et al., 1988). This is partly because of 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 USA, ranging from 300 mg/day to 1 000 mg/day depending on individual food preferences (IOM, 1997).

3.2. Dietary intake

EFSA estimated dietary intakes of phosphorus from food consumption data from the EFSA Comprehensive European Food Consumption Database (EFSA, 2011a), classified according to the food classification and description system FoodEx2 (EFSA, 2011b). Food consumption data from 13 dietary surveys from nine European Union (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 from Finland, France, Germany, Italy, the Netherlands, Sweden and the UK was used to calculate phosphorus intake 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 phosphorus intake estimates for 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 the event 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

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.

and 85 %. A phosphorus value was missing for all included countries for 665 consumed food items, for which imputation of missing composition values was undertaken by EFSA. Phosphorus intake calculations were performed only on subjects with at least two reporting days. EFSA intake estimates are based on the consumption of foods, either fortified or not (i.e. without consideration of dietary supplements).

Food consumption data of infants (aged 1 to < 12 months in the Italian INRAN-SCAI survey, 4 to < 12 months in the UK DNSIYC survey, 6 months in the Finnish DIPP study and 6 to < 12 months in the German VELs survey, for full names of all surveys, see Abbreviations) were provided by four studies. The consumption of human milk was taken into account if the amount of human milk consumed (Italian INRAN-SCAI survey and UK DNSIYC survey) or the number of breast milk consumption events (German VELs survey) were reported. In the case of the Italian INRAN-SCAI survey, the data provider had estimated the human milk consumption prior to submitting the data to EFSA 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 of the number of breast milk consumption events 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.

For both sexes combined, average phosphorus intake ranged from 265 to 531 mg/day (102–154 mg/MJ) in infants (< 1 year of age, four surveys), from 641 to 973 mg/day (149–207 mg/MJ) in children aged 1 to < 3 years (five surveys), from 750 to 1 202 mg/day (133–206 mg/MJ) in children aged 3 to < 10 years (seven surveys), from 990 to 1 601 mg/day (131–196 mg/MJ) in children aged 10 to < 18 years (seven surveys) and from 1 000 to 1 767 mg/day (149–207 mg/MJ) in adults (≥ 18 years) (eight surveys). Average daily intake was, in most cases, slightly higher in males (Appendix B) than in females (Appendix C), mainly because of larger quantities of food consumed per day.

The main food groups contributing to phosphorus intake 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 INCA2 survey (Afssa, 2009), the Irish NANS (IUNA, 2011), the Finnish FINDIET 2012 Survey (Helldán et al., 2013), the Italian INRAN-SCAI survey (Sette et al., 2011), the Dutch National Food Consumption Survey (van Rossum et al., 2011) and the Swedish national survey Riksmaten (Amcoff et al., 2012) (Table 2). Values below 100 % indicate that EFSA’s intake estimates are lower than published values and values above 100 % indicate the opposite.

Table 2: EFSA's average phosphorus intake estimates, expressed as percentages of published intake

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)
Netherlands	91–93 (Dutch National Food Consumption 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 by 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 % than 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 formulae 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 comparing the EFSA phosphorus intake estimates with published values for VELs before and after this change, the difference in estimated phosphorus intakes increases from < 5 % to about 20 %.

For the Irish and Swedish surveys, the EFSA intake estimates were higher by about 6–15 % than 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 with the Irish situation. In addition, the Irish composite dishes were highly disaggregated to their ingredients in the dataset submitted to EFSA.

Uncertainties in the estimates of all countries may be caused by inaccuracies in mapping food consumption data according to the FoodEx2 classification, analytical errors or errors in the estimation of the concentration in foods in the food composition databases, the use of borrowed phosphorus values from other countries in the food composition databases, and the replacement of missing phosphorus values by available values for similar foods or food groups in the phosphorus intake estimation process. These uncertainties may, in principle, lead to estimates of phosphorus intake that are both too high and too low. It is not possible to conclude which of these intake estimates (i.e. the EFSA intake estimate or the published one) would be closer to the actual phosphorus intake.

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 the US Institute of Medicine (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 (RI) of 600 mg/day had been set earlier (Nordic Council of Ministers, 2004). For the 5th edition of the Nordic Nutrition Recommendations (NNR 2012), it was considered that there are no new data indicating that this value should be changed (Nordic Council of Ministers, 2014).

The German-speaking countries (D-A-CH, 2015) considered that data from which RIs could be derived are much rarer for phosphorus than for calcium. An AR for adults was estimated to be 580 mg/day according to the IOM (1997). Given a coefficient of variation (CV) of 10 %, the RI was set at 700 mg/day.

The French Food Safety Authority (Afssa, 2001) used a factorial approach to calculate the AR. Urinary and faecal losses were estimated in accordance with Wilkinson (1976), Nordin (1989) and 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 IOM (1997) used the lower end of the normal adult serum inorganic phosphorus range (0.87 mmol/L) and considered that this value would be obtained by an intake of \approx 580 mg (\approx 19 mmol)/day (Nordin, 1989), which was considered 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 intake should correspond, on a molar basis, to that 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, however, revised 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 to phosphorus ratio (weight by weight) of less than 0.5:1 should be avoided. It was suggested that the lower limit of the RDA for calcium be applied as the lower limit of the Adequate Range of Intake for phosphorus. Allowing for a calcium to phosphorus ratio of 0.5:1 (weight by weight), the upper limit of the Adequate Range of Intake for phosphorus 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 the 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 Intake for phosphorus for adults over 50 years was calculated on the basis of a calcium to phosphorus ratio (weight by weight) of 0.7:1. The lower limit equated to that of adults up to the age of 50 years.

The UK Committee on Medical Aspects of Food Policy (COMA) (DH, 1991) took the view that requirements should be set at a ratio of 1 mmol phosphorus to 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.

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

	D-A-CH (2015)	NCM (2014)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) ^(a)	DH (1991)
Age (years)	≥ 19	18–20	20–64	≥ 19	≥ 18	19–50	≥ 19
PRI							
Men (mg/day)	700	700	750	700	550	700–1 400	550
Women (mg/day)	700	700	750 ^(b)	700	550	700–1 400	550
Age (years)		≥ 21	65–74			≥ 50	
PRI							
Men (mg/day)		600	750			700–1 150 ^(d)	
Women (mg/day)		600	800 ^(c)			700–1 150 ^(d)	
Age (years)			≥ 75				
PRI							
Men (mg/day)			800				
Women (mg/day)			800				

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council; PRI, Population Reference Intake.

(a): Adequate Range of Intake.

(b): 20–55 years.

(c): > 55 years.

(d): Lower limit of the Adequate Range of Intake for adults below the age of 50 years is also considered adequate for this age group.

4.2. Infants and children

The Nordic countries considered that RIs for phosphorus should correspond, on a molar basis, to those for calcium (Nordic Council of Ministers, 2004). For NNR 2012, it was considered that there are no new data indicating that these values should be changed (Nordic Council of Ministers, 2014).

For puberty and adolescence, the German-speaking countries (D-A-CH, 2015) considered that the requirement for phosphorus is higher compared with that in adults because of new tissue formation and bone growth. Accordingly, an RI of 1 250 mg/day was set for children and adolescents from 10 to below 19 years of age.

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

For infants aged 0 to 6 months, the IOM (1997) set an AI of 100 mg (3.2 mmol)/day based on a mean breast milk intake of 780 mL/day (Butte et al., 1984a; Allen et al., 1991) and an average phosphorus concentration of human milk of 124 mg/L (Atkinson et al., 1995). For infants aged 6–12 months, the AI of 275 mg (8.9 mmol)/day was based on the phosphorus intake from breast milk and solid foods. An average intake of 75 mg/day was calculated from an average human milk concentration of 124 mg/L (Atkinson et al., 1995) and a mean breast milk intake of 600 mL/day (Dewey et al., 1984). The contribution from solid foods was estimated to be 200 mg/day from data on 40 infants fed standard infant formula and solid food (Specker et al., 1997), which was comparable to estimations from the 1976–1980 NHANES II for infants aged 7–12 months (Montalto and Benson, 1986). For 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 (1.7 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 the known composition of muscle (Pennington, 1994). The urinary loss was calculated to be 213 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 (2.0 mmol)/day was derived. The assumptions for efficiency of phosphorus absorption and urinary loss of phosphorus are identical to that used for 1- to 3-year-old children. 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 to be 565 mg (18.2 mmol)/day using the equation from Lemann (1996). Absorption efficiency was averaged to 60–80 % (Lutwak et al., 1964; Greger et al., 1978) and a midpoint 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 9- to 18-year-old children.

The SCF (1993) suggested that phosphorus intake should correspond, on a molar basis, to that 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 to phosphorus ratio. For infants aged 6–12 months, a calcium to phosphorus ratio (weight by weight) of 1:1 was applied, whereas the calcium to phosphorus ratio was 0.5:1 to 1:1 (weight by weight) for children and adolescents.

The UK COMA (DH, 1991) took the view that requirements should be set at a molar calcium to phosphorus ratio of 1:1, 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 the DRVs for phosphorus for infants and children proposed by various committees can be found in Table 4.

Table 4: Overview of Dietary Reference Values for phosphorus for children

	D-A-CH (2015)	NCM (2014)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) ^(a)	DH (1991)
Age (months)	4–< 12	6–11	6–12	7–12	6–11	6–12	0–12
PRI (mg/day)	300	420	275 ^(b)	275 ^(b)	300	400	400
Age (years)	1–< 4	1–5	1–3	1–3	1–3	1–4	1–3
PRI (mg/day)	500	470	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)	7–< 10	6–9	7–9		7–10	7–10	7–10
PRI (mg/day)	800	540	600 ^(c)		450	600–1 200	450
Age (years)	10–< 19	10–17	10–12	9–18			
PRI (mg/day)	1 250	700	830 ^(c)	1 250			
Age (years)			13–15		11–17	10–16	11–18
PRI							
Boys (mg/day)			830 ^(c)		775	900–1 800	775
Girls (mg/day)			800 ^(c)		625	700–1 400	625
Age (years)			16–19			16–19	
PRI							
Boys (mg/day)			800 ^(c)			800–1 600	
Girls (mg/day)			800 ^(c)			700–1 400	

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council; PRI, Population Reference Intake.

(a): Adequate Range of Intake.

(b): Adequate Intake (AI).

(c): As reported on page 507 of the report.

4.3. Pregnancy

The German-speaking countries (D-A-CH, 2015) estimated that during pregnancy an average of 60 mg/day of phosphorus must be provided to meet the needs of pregnancy. Taking into account intestinal absorption, an additional allowance of 100 mg/day was set compared with that for non-pregnant women.

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

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

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

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

An overview of DRVs for phosphorus for pregnant women proposed by various committees can be found in Table 5.

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

	D-A-CH (2015)	NCM (2014)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) ^(a)	DH (1991)
Age (years)	< 19			14–18			
PRI (mg/day)	1 250	700	800 ^(b)	1 250	550	800–1 600	550
Age (years)	≥ 19			19–50			
PRI (mg/day)	800			700			

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council; PRI, Population Reference Intake.

(a): Adequate Range of Intake.

(b): Third trimester.

4.4. Lactation

The German-speaking countries (D-A-CH, 2015) estimated that an additional amount of phosphorus of 90–120 mg/day was needed during lactation. Taking into account intestinal absorption an additional allowance of 200 mg/day was set compared to that for non-lactating women.

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

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

The SCF (1993) suggested that phosphorus intake should correspond, on a molar basis, to that for calcium and a rounded PRI value was proposed accordingly.

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

The UK COMA (DH, 1991) took the view that requirements should be set at a ratio of 1 mmol phosphorus to 1 mmol calcium, 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 lactating women proposed by various committees can be found in Table 6.

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

	D-A-CH (2015)	NCM (2014)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992) ^(a)	DH (1991)
Age (years)	< 19			14–18			
PRI (mg/day)	1 250	900	850	1 250	950	900–1 800	+ 440
Age (years)	≥ 19			19–50			
PRI (mg/day)	900			700			

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council; PRI, Population Reference Intake.

(a): Adequate Range of Intake.

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

5.1. Indicators of phosphorus requirement

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

5.2. Balance studies on phosphorus

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

Few phosphorus balance studies are available in comparison with studies on other minerals, such as calcium, partly because phosphorus isotopes cannot be safely used for kinetic studies. Thus, the study of the regulation of phosphorus homeostasis has often been considered as subordinate to that of calcium. Phosphorus balance, like calcium balance, is maintained by intestinal absorption, renal excretion and bone accretion. However, there are important differences between phosphorus and calcium balance. Dietary phosphorus, which grossly parallels dietary protein, is present in abundance in most foods; this is in contrast to calcium, which is restricted to relatively few food groups. Dietary phosphorus is absorbed more efficiently than dietary calcium. Thus, phosphorus absorption is not a limiting factor, whilst renal elimination may be a limiting factor at intakes that result in a filtered glomerular load exceeding the renal tubular reabsorption capacity.

5.2.1. Balance studies in adults

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

Ohlson et al. (1952) evaluated phosphorus balance in a multicentre 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 associated with a positive balance was 1 150 mg/day.

Marshall et al. (1976) reported on balance studies that aimed to evaluate calcium, magnesium and phosphorus requirements in adults. Participants were administered a constant diet for two weeks. Phosphorus intake ranged from about 400 mg/day to 3 800 mg/day. 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 concluded 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 6 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 during only the “low” calcium (200 mg/day) and the “normal” phosphorus (800 mg/day) diet period. Under all other dietary conditions, phosphorus balance was zero or positive. In particular, under conditions of “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 final 12 days of each 28-day diet period and duplicate samples of the diet were analysed. A phosphorus balance of zero 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 1-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 because of 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, 6-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 for calcium, magnesium and phosphorus in Japanese adults. A total of 109 volunteers (23 males, 86 females), ranging from 18 to 28 years of age, took part in mineral balance studies; the duration of these studies 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 were 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 in 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 weight¹⁰ per day (95 % CI 16.7–17.8 mg/kg standard body weight per day). 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 short equilibration period in this study.

The Panel notes that the available phosphorus balance studies are rather heterogeneous 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 calcium and other dietary factors possibly affecting phosphorus metabolism, that only a few studies were conducted under metabolic ward conditions and that zero phosphorus balance may be achieved across a wide range of intakes and across a wide range of dietary molar calcium to phosphorus ratios. 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/day) and after a 9-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 body mass index of 22 kg/m².

The Panel notes that the data available are 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. Between weeks 5 and 36 of gestation, a maximum of six 7-day balance periods were completed on each subject. Average calcium intake was $1\,370 \pm 290$ mg/day. At an estimated phosphorus intake of $1\,340 \pm 280$ 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 7-day experimental period to another was observed.

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

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 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 regarding 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 the present Opinion, 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 to 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 relating phosphorus intake to health outcomes will be considered for this section, though the Panel notes the difficulty in assessing phosphorus intake as a result of inaccuracies in food composition tables (Section 3.1) and variations in phosphorus absorption due to nutrient interactions (see Sections 2.3.1 and 2.3.7).

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 the 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 aged 8 years. Yin et al. (2010) investigated bone mass in the same population at 16 years of age. 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 ages 8 and 16 years, dual-energy X-ray absorptiometry (DXA) was performed. As not all children in the cohort underwent a scan at both 8 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 $2\,767 \pm 1\,655$ mg/day (Jones et al., 2000) and $2\,314 \pm 898$ mg/day (Yin et al., 2010). At age 8 years, the BMD of the femoral neck and lumbar spine were positively associated ($p = 0.01$ and $p = 0.001$) with the 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 than 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 $1\,339 \pm 338$ mg/day, which is comparable to the mean daily intake of $1\,112 \pm 299$ mg/day measured in women in the UK (Henderson et al., 2003). Bone mineral mass of the children was measured at 9 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. During 8 years of follow-up, dietary data and data on sedentary activities (i.e. time not spent in physical activity) of the children were collected. Dietary intake was assessed at nine collection points (from 2.3 to 8 years of age) by means of in-home dietary interviews. Bone mineral indices were measured by DXA when children were 8 years old. Correlations between phosphorus intake and bone mineral content (BMC) ($r = 0.33$) and BMD ($r = 0.30$) were significant ($p < 0.05$). In a multivariate regression model predicting BMC at 8 years of age, phosphorus intake showed a small but significant contribution to the model ($\beta = 0.11$; $R^2 = 0.05$; $p = 0.01$). However, calcium and 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 8 years and that phosphorus intake during childhood may be associated with BMD at the age of 8 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.

5.4.1.1. Dietary calcium to phosphorus ratio in relation to bone health

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 phosphorus during growth has been acknowledged (EFSA NDA Panel, 2014). In adults, there are findings that suggest that the ratio of these two minerals in the diet may have a 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 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 phosphorus molar ratio in adults for bone health, but notes that calcium and phosphorus are present in bone in a molar ratio of approximately 1.6:1 to 1.8:1 (Section 2.3.3.1).

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 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 with 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 with 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 in the SU.VI.MAX trial (SUPplémentation en VITamines et Minéraux Anti-oXydants). In almost 8 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 ($p_{\text{trend}} = 0.04$), 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 8 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, $p_{\text{trend}} = 0.77$).

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 the incidence of bladder cancer ($p_{\text{trend}} = 0.40$). The multivariate adjusted RR (not adjusted for calcium) of the highest quintile (median phosphorus intake 1 728 mg/day) compared with the lowest quintile (median phosphorus intake 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 3.7 years of follow-up, 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 ($p_{\text{trend}} = 0.005$). 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 sub-group of women with high-risk adenomas, no association was observed. This sub-group ($n = 175$) covered women diagnosed with large adenomas (> 1 cm in diameter), adenomas with severe dysplasia and multiple adenomas (three or more), 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 criteria 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, kidney diseases or CVD participating in NHANES III (1988–1994). Dietary phosphorus intake, assessed by 24-hour dietary recall, was expressed as the absolute intake and as 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) = 2.23, 95 % CI = 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 = 2.27, 95 % CI = 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 = 3.39, 95 % CI = 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 (Anonymous, 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 CVD. 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 % increase in estimated dietary phosphorus intake was associated with an increase in left ventricular mass of 1.06 g (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. Furthermore, higher dietary phosphorus intake was associated with a lower risk of developing future hypertension after adjustment for non-dietary confounders (HR = 0.80, 95 % CI = 0.80–1.00, comparing extreme quintiles, $p_{\text{trend}} = 0.02$); however, this association was no longer significant after adjustment for dietary factors (HR = 1.01, 95 % CI = 0.82–1.23, $p_{\text{trend}} = 0.88$). After adjustment, phosphorus only from dairy products, but not from other sources, was associated with lower baseline blood pressure and reduced risk of incident hypertension. HRs (95 % CIs) comparing extreme quintiles were 0.86 (95 % CI = 0.76–0.97, $p_{\text{trend}} = 0.01$) for phosphorus from dairy foods and 1.04 (95 % CI = 0.93–1.17, $p_{\text{trend}} = 0.48$) 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 and 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 themselves, 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

The Panel considers that there are currently no reliable biomarkers of phosphorus intake and status that may be used for deriving the requirement for phosphorus (Section 2.4). In addition, the Panel notes that estimations of phosphorus absorption from the diet (Section 2.3.1), as well as losses of phosphorus via urine (Section 2.3.6.1) and faeces (Section 2.3.6.2), vary over a wide range, so that the factorial approach cannot be used for deriving the requirement for phosphorus. The Panel also considers that data on balance studies and on phosphorus intake and health outcomes cannot be used for setting DRVs for phosphorus.

Instead, the Panel proposes to use the calcium to phosphorus ratio in the whole body to set DRVs for phosphorus, taking into account the DRVs for calcium (EFSA NDA Panel, 2015). The Panel notes that data on the molar ratio of calcium to phosphorus in the intact bone of healthy adults, used for extrapolation of the whole-body calcium to phosphorus ratio (Section 2.3.3.1), and data from whole-body calcium and phosphorus measurements in Caucasian men and women (Section 2.3.3.1) indicate that the calcium to phosphorus molar ratio in the whole body ranges from 1.4:1 to 1.9:1.

In adults, the data on net phosphorus absorption have been reported to vary over a wide range (Section 2.3.1). The Panel notes that the fractional absorption of phosphorus is higher than that of calcium (EFSA NDA Panel, 2015), but the Panel considers that the actual amounts of calcium and phosphorus that are available for absorption from the diet and may be retained in the body cannot be determined. In the absence of this information, the Panel proposes to set DRVs for phosphorus based solely on the range of the molar ratio of calcium to phosphorus 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. Based on the AI (for infants aged 7–11 months) and the PRIs (for all other ages) for calcium (EFSA NDA Panel, 2015), and considering a molar calcium to phosphorus ratio of 1.4:1 to 1.9:1, amounts of phosphorus (in mg/day) were calculated (Appendix F). The Panel chose the lower bound of this range (i.e. a ratio of 1.4:1 which results in the higher phosphorus intake value) for deriving an AI for phosphorus, taking into account estimated phosphorus intakes in Western countries, which are considerably higher (Section 3.2) than the values calculated in Appendix F. AIs for all age groups were set after rounding to the nearest

10 mg/day (Table 7). The Panel considers that the AIs proposed for infants and children cover the quantity of phosphorus estimated for accretion in bone in these age groups (Section 2.3.4).

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 for additional dietary phosphorus during pregnancy and lactation, provided intake is close to the AI for adults (see Section 5.3). Therefore, the Panel concludes that additional dietary phosphorus is not required for pregnant and lactating women.

CONCLUSIONS

The Panel derived DRVs for phosphorus based on the AI (for infants aged 7–11 months) and the PRIs (for all other age groups) for calcium. The Panel used data on the calcium to phosphorus ratio in the bone of healthy men and women and adjusted these data for the proportion of phosphorus present outside bone. In addition, data on whole-body contents of calcium and phosphorus in Caucasian adults were used to calculate molar calcium to phosphorus ratios in the whole body. These data indicate that the calcium to phosphorus molar ratio in the whole body ranges from 1.4:1 to 1.9:1. The Panel considered that the available data are insufficient to derive ARs and PRIs for phosphorus and, therefore, the Panel proposed that AIs are set for all population groups. For this, the Panel chose the lower bound of the range (i.e. a calcium to phosphorus molar ratio in the whole body of 1.4:1, which results in the higher phosphorus intake value) for setting an AI for phosphorus (Table 7), taking into account estimated phosphorus intakes in Western countries, which are considerably higher than the values calculated on the basis of this range. It was considered that the AI for adults should also apply to pregnant and lactating women.

Table 7: Summary of Adequate Intakes for phosphorus

Age	Adequate Intake (mg/day)
7–11 months	160
1–3 years	250
4–10 years	440
11–17 years	640
Adults \geq 18 years ^(a)	550

(a): Including pregnant and lactating women.

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 that research be undertaken on the effect of dietary phosphorus intake on long-term health outcomes and the risk of chronic disease.

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

REFERENCES

- Afssa (Agence française de sécurité sanitaire des aliments), 2001. Apports nutritionnels conseillés pour la population française. Editions Tec&Doc, Paris, France, 605 pp.
- Afssa (Agence française de sécurité sanitaire des aliments), 2009. Étude Individuelle Nationale des Consommations Alimentaires 2 (INCA 2) (2006-2007). Rapport. 228 pp.
- Alizadeh Naderi AS and Reilly RF, 2010. Hereditary disorders of renal phosphate wasting. *Nature Reviews Nephrology*, 6, 657-665.
- Allen JC, Keller RP, Archer P and Neville MC, 1991. Studies in human lactation: milk composition and daily secretion rates of macronutrients in the first year of lactation. *American Journal of Clinical Nutrition*, 54, 69-80.
- Alonso A, Nettleton JA, Ix JH, de Boer IH, Folsom AR, Bidulescu A, Kestenbaum BR, Chambless LE and Jacobs DR, Jr., 2010. Dietary phosphorus, blood pressure, and incidence of hypertension in the atherosclerosis risk in communities study and the multi-ethnic study of atherosclerosis. *Hypertension*, 55, 776-784.
- Amcoff E, Edberg A, Enghardt Barbieri H, Lindroos A, Nälsén C, Pearson M and Warensjö Lemming E (Livsmedelsverket), 2012. Riksmaten – vuxna 2010–11. Livsmedels- och näringsintag bland vuxna i Sverige. Resultat från matvaneundersökning utförd 2010–11. 180 pp.
- Anderson J, 2005. Phosphorus. In: *Encyclopedia of Human Nutrition*. Eds Caballero B, Allen L and Prentice A. Elsevier, Oxford, UK, 486-490.
- Anonymous, 1994. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988-94. Series 1: programs and collection procedures. *Vital and Health Statistics. Series 1: Programs and Collection Procedures*, 1-407.
- Ashe JR, Schofield FA and Gram MR, 1979. The retention of calcium, iron, phosphorus, and magnesium during pregnancy: the adequacy of prenatal diets with and without supplementation. *American Journal of Clinical Nutrition*, 32, 286-291.
- Atkinson SA, Radde IC, Chance GW, Bryan MH and Anderson GH, 1980. Macro-mineral content of milk obtained during early lactation from mothers of premature infants. *Early Human Development*, 4, 5-14.
- Atkinson SA, Alston-Mills BP, Lönnerdal B and Neville MC, 1995. B. Major minerals and ionic constituents of human and bovine milks. In: *Handbook of milk composition*. Ed Jensen RJ. Academic Press, San Diego, CA, USA, 593-619
- Audi G, Bersillon O, Blachot J and Wapstra AH, 2003. The NUBASE evaluation of nuclear and decay properties. *Nuclear Physics A*, 729, 3-128.
- Baer JD, Fong AKH, Novotny JA and Oexmann MJ, 1999. Compartmental modeling, stable isotopes, and balance studies. In: *Well-controlled diet studies in humans: A practical guide to design and management*. Eds Dennis BH, Ershow AG, Obarzanek E and Clevidence BA. American Dietetic Association, Chicago, IL, USA, 238-254.
- Bansal VK, 1990. Serum Inorganic Phosphorus. In: *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd edition. Eds Walker HK, Hall WD and Hurst JW. Butterworths, Boston, MA, USA, 895-899.
- Bergwitz C and Jüppner H, 2010. Regulation of phosphate homeostasis by PTH, vitamin D, and FGF23. *Annual Review of Medicine*, 61, 91-104.
- Bergwitz C and Jüppner H, 2011. Phosphate sensing. *Advances in Chronic Kidney Disease*, 18, 132-144.
- Berndt T and Kumar R, 2007. Phosphatonins and the regulation of phosphate homeostasis. *Annual Review of Physiology*, 69, 341-359.

- Berndt T and Kumar R, 2009. Novel mechanisms in the regulation of phosphorus homeostasis. *Physiology (Bethesda)*, 24, 17-25.
- Biber J, Harnando N and Forster I, 2013. Phosphate transporters and their function. *Annual Review of Physiology*, 75, 535-550.
- Bijovet OLM, 1969. Regulation of plasma phosphate concentration to renal tubular reabsorption of phosphate. *Clinical Science*, 37, 23-26.
- Bindels RJM, Hoenderop JGJ and Biber J, 2012. Transport of calcium, magnesium, and phosphate. In: Brenner & Rector's *The Kidney*, 9th edition. Eds Taal MW, Chertow GM, Marsden PA, Skorecki K, Yu ASL and Brenner BM. Saunders, Philadelphia, PA, USA, 226-251.
- Bjorklund KL, Vahter M, Palm B, Grander M, Lignell S and Berglund M, 2012. Metals and trace element concentrations in breast milk of first time healthy mothers: A biological monitoring study. *Environmental Health: A Global Access Science Source*, 11.
- Bounds W, Skinner J, Carruth BR and Ziegler P, 2005. The relationship of dietary and lifestyle factors to bone mineral indexes in children. *Journal of the American Dietetic Association*, 105, 735-741.
- Brickman AS, Coburn JW, Massry SG and Norman AW, 1974. 1,25 Dihydroxy-vitamin D3 in normal man and patients with renal failure. *Annals of Internal Medicine*, 80, 161-168.
- Brickman AS, Hartenbower DL, Norman AW and Coburn JW, 1977. Actions of 1 alpha-hydroxyvitamin D3 and 1,25-dihydroxyvitamin D3 on mineral metabolism in man. I. Effects on net absorption of phosphorus. *American Journal of Clinical Nutrition*, 30, 1064-1069.
- Brot C, Jorgensen N, Madsen OR, Jensen LB and Sorensen OH, 1999. Relationships between bone mineral density, serum vitamin D metabolites and calcium:phosphorus intake in healthy perimenopausal women. *Journal of Internal Medicine*, 245, 509-516.
- Brunelli SM and Goldfarb S, 2007. Hypophosphatemia: clinical consequences and management. *Journal of the American Society of Nephrology*, 18, 1999-2003.
- Brunette MG, Letendre S and Allard S, 1986. Phosphate transport through placenta brush border membrane. *Advances in Experimental Medicine and Biology*, 208, 543-548.
- Butte NF, Garza C, Smith EO and Nichols BL, 1984a. Human milk intake and growth in exclusively breast-fed infants. *Journal of Pediatrics*, 104, 187-195.
- Butte NF, Garza C, Johnson CA, Smith EO and Nichols BL, 1984b. Longitudinal changes in milk composition of mothers delivering preterm and term infants. *Early Human Development*, 9, 153-162.
- Calvo MS, Kumar R and Heath H, 3rd, 1988. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. *Journal of Clinical Endocrinology and Metabolism*, 66, 823-829.
- Calvo MS and Tucker KL, 2013. Is phosphorus intake that exceeds dietary requirements a risk factor in bone health? *Annals of the New York Academy of Sciences*, 1301, 29-35.
- Calvo MS and Uribarri J, 2013. Contributions to total phosphorus intake: all sources considered. *Seminars in Dialysis*, 26, 54-61.
- Chan JM, Pietinen P, Virtanen M, Malila N, Tangrea J, Albanes D and Virtamo J, 2000. Diet and prostate cancer risk in a cohort of smokers, with a specific focus on calcium and phosphorus (Finland). *Cancer Causes and Control*, 11, 859-867.
- Chang AR, Lazo M, Appel LJ, Gutierrez OM and Grams ME, 2014. High dietary phosphorus intake is associated with all-cause mortality: results from NHANES III. *American Journal of Clinical Nutrition*, 99, 320-327.
- Christov M and Jüppner H, 2013. Insights from genetic disorders of phosphate homeostasis. *Seminars in Nephrology*, 33, 143-157.

- Consolazio CF, Matoush LO, Nelson RA, Harding RS and Canham JE, 1963. Excretion of sodium, potassium, and iron in human sweat and the relationship of each to balance and requirements. *Journal of Nutrition*, 79, 407-415.
- Corbridge DEC, 2013. *Phosphorus: Chemistry, Biochemistry and Technology*. Sixth edition. CRC Press, Boca Raton, FL, USA, 1439 pp.
- D-A-CH (Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, Schweizerische Gesellschaft für Ernährung), 2015. *Referenzwerte für die Nährstoffzufuhr*. 2. Auflage, 1. Ausgabe. DGE, Bonn, Germany.
- de Boer IH, Rue TC and Kestenbaum B, 2009. Serum phosphorus concentrations in the third National Health and Nutrition Examination Survey (NHANES III). *American Journal of Kidney Diseases*, 53, 399-407.
- de Menezes FH, de Castro LC and Damiani D, 2006. Hypophosphatemic rickets and osteomalacia. *Arquivos Brasileiros de Endocrinologia & Metabologia*, 50, 802-813.
- Delgado-Andrade C, Seiquer I, García MM, Galdó G and Navarro MP, 2011. Increased Maillard reaction products intake reduces phosphorus digestibility in male adolescents. *Nutrition*, 27, 86-91.
- Deurenberg P, Pieters JJ and Hautvast JG, 1990. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *British Journal of Nutrition*, 63, 293-303.
- Dewey KG, Finley DA and Lönnerdal B, 1984. Breast milk volume and composition during late lactation (7-20 months). *Journal of Pediatric Gastroenterology and Nutrition*, 3, 713-720.
- DH (Department of Health), 1991. *Dietary reference values for food energy and nutrients for the United Kingdom. Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy*. HMSO, London, UK, 212 pp.
- Eeuwijk J, Oordt A and Vonk Noordegraaf-Schouten M, 2012. Literature search and review related to specific preparatory work in the establishment of Dietary Reference Values for phosphorus, sodium and chloride. Project developed on the procurement project CT/EFSA/NDA/2012/01. EFSA Supporting publication 2013:EN-502, 388 pp.
- EFSA (European Food Safety Authority), 2005. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of phosphorus. *The EFSA Journal* 233, 19 pp. doi:10.2903/j.efsa.2005.233
- EFSA (European Food Safety Authority), 2011a. Use of the EFSA Comprehensive European Food Consumption Database in exposure assessment. *EFSA Journal* 2011;9(3):2097, 34 pp. doi:10.2903/j.efsa.2011.2097
- EFSA (European Food Safety Authority), 2011b. Report on the development of a food classification and description system for exposure assessment and guidance on its implementation and use. *EFSA Journal* 2011;9(12):2489, 84 pp. doi:10.2903/j.efsa.2011.2489
- EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2014. Scientific Opinion on the essential composition of infant and follow-on formulae. *EFSA Journal* 2014;12(7):3760, 106 pp. doi:10.2903/j.efsa.2013.3760
- EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2015. Scientific Opinion on Dietary Reference Values for calcium. *EFSA Journal* 2015;13(5):4101, 84 pp. doi:10.2903/j.efsa.2015.4101
- Ellis KJ, 1990. Reference man and woman more fully characterized. Variations on the basis of body size, age, sex, and race. *Biological Trace Element Research*, 26-27, 385-400.
- Eto N, Tomita M and Hayashi M, 2006. NaPi-mediated transcellular permeation is the dominant route in intestinal inorganic phosphate absorption in rats. *Drug Metabolism and Pharmacokinetics*, 21, 217-221.

- FAO/WHO (Food and Agriculture Organization/World Health Organization), 1974. Toxicological evaluation of certain food additives including anticaking agents, antimicrobials, antioxidants, emulsifiers, and thickening agents. 53A, FAO Nutrition Meetings Report Series, 469-485.
- Farrow EG and White KE, 2010. Recent advances in renal phosphate handling. *Nature Reviews Nephrology*, 6, 207-217.
- Fenton TR, Lyon AW, Eliasziw M, Tough SC and Hanley DA, 2009. Phosphate decreases urine calcium and increases calcium balance: a meta-analysis of the osteoporosis acid-ash diet hypothesis. *Nutrition Journal*, 8, 41.
- Fomon SJ, Haschke F, Ziegler EE and Nelson SE, 1982. Body composition of reference children from birth to age 10 years. *American Journal of Clinical Nutrition*, 35, 1169-1175.
- Forster I, Hernando N, Sorribas V and Werner A, 2011. Phosphate transporters in renal, gastrointestinal, and other tissues. *Advances in Chronic Kidney Diseases*, 18, 63-76.
- Gaasbeek A and Meinders A, 2005. Hypophosphatemia: an update on its etiology and treatment. *The American Journal of Medicine*, 118, 1094-1101.
- Gibson RS, 2005. *Principles of nutritional assessment*, 2nd edition. Oxford University Press, New York, NY, USA, 928 pp.
- Gidrewicz DA and Fenton TR, 2014. A systematic review and meta-analysis of the nutrient content of preterm and term breast milk. *BMC Pediatrics*, 14, 216.
- Greenberg BG, Winters RW and Graham JB, 1960. The normal range of serum inorganic phosphorus and its utility as a discriminant in the diagnosis of congenital hypophosphatemia. *Journal of Clinical Endocrinology and Metabolism*, 20, 364-379.
- Greger JL, Baligar P, Abernathy RP, Bennett OA and Peterson T, 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *American Journal of Clinical Nutrition*, 31, 117-121.
- Gross SJ, David RJ, Bauman L and Tomarelli RM, 1980. Nutritional composition of milk produced by mothers delivering preterm. *Journal of Pediatrics*, 96, 641-644.
- Guéguen L, 1982. Les phosphates dans l'alimentation humaine. *Médecine et Nutrition*, 18, 237-245.
- Gutierrez OM, 2013. The connection between dietary phosphorus, cardiovascular disease, and mortality: where we stand and what we need to know. *Advances in Nutrition*, 4, 723-729.
- Health Council of the Netherlands, 2000. *Dietary reference intakes: calcium, vitamin D, thiamin, riboflavin, niacin, pantothenic acid, and biotin*. 180 pp.
- Heaney RP and Skillman TG, 1971. Calcium metabolism in normal human pregnancy. *Journal of Clinical Endocrinology and Metabolism*, 33, 661-670.
- Heaney RP and Recker RR, 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *Journal of Laboratory and Clinical Medicine*, 99, 46-55.
- Heaney RP and Recker RR, 1987. Calcium supplements: anion effects. *Bone and Mineral*, 2, 433-439.
- Heaney RP and Nordin BE, 2002. Calcium effects on phosphorus absorption: implications for the prevention and co-therapy of osteoporosis. *Journal of the American College of Nutrition*, 21, 239-244.
- Heaney RP, 2012. Phosphorus. In: *Present Knowledge in Nutrition*. Eds Erdman JW, Jr, Macdonald IA and Zeisel SH. John Wiley & Sons, Washington, DC, USA, 447-458.
- Helldán A, Raulio S, Kosola M, Tapanainen H, Ovaskainen ML and Virtanen S, 2013. Finravinto 2012 - tutkimus - The National FINDIET 2012 Survey. THL. Raportti 16/2013, 217 pp.

- Henderson L, Irving K and Gregory J, 2003. The National Diet and Nutrition Survey: adults aged 19 to 64 years. Vitamin and mineral intake and urinary analytes. 3, The Stationery Office, London, UK.
- Hoppu U, Lehtisalo J, Tapanainen H and Pietinen P, 2010. Dietary habits and nutrient intake of Finnish adolescents. *Public Health Nutrition*, 13, 965-972.
- Hruska KA, Mathew S, Lund R, Qiu P and Pratt R, 2008. Hyperphosphatemia of chronic kidney disease. *Kidney International*, 74, 148-157.
- Hu MC, Shi M, Zhang J, Pastor J, Nakatani T, Lanske B, Razzaque MS, Rosenblatt KP, Baum MG, Kuro-o M and Moe OW, 2010. Klotho: a novel phosphaturic substance acting as an autocrine enzyme in the renal proximal tubule. *FASEB Journal*, 24, 3438-3450.
- Hure A, Young A, Smith R and Collins C, 2009. Diet and pregnancy status in Australian women. *Public Health Nutrition*, 12, 853-861.
- Husain SM and Mughal MZ, 1992. Mineral transport across the placenta. *Archives of Disease in Childhood*, 67, 874-878.
- IOM (Institute of Medicine), 1997. Dietary Reference Intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. National Academy Press, Washington, DC, USA, 454 pp.
- Ito S, Ishida H, Uenishi K, Murakami K and Sasaki S, 2011. The relationship between habitual dietary phosphorus and calcium intake, and bone mineral density in young Japanese women: a cross-sectional study. *Asia Pacific Journal of Clinical Nutrition*, 20, 411-417.
- IUNA (Irish Universities Nutrition Alliance), 2011. National Adult Nutrition Survey. 40 pp.
- Jones G, Riley MD and Dwyer T, 2000. Maternal diet during pregnancy is associated with bone mineral density in children: a longitudinal study. *European Journal of Clinical Nutrition*, 54, 749-756.
- Jubiz W, Canterbury JM, Reiss E and Tyler FH, 1972. Circadian rhythm in serum parathyroid concentration in human subjects: correlation with serum calcium, phosphate, albumin and growth hormone levels. *Journal of Clinical Investigation*, 51, 2040-2046.
- Jüppner H, 2007. Novel regulators of phosphate homeostasis and bone metabolism. *Therapeutic Apheresis and Dialysis*, 11, S3-S22.
- Kalantar-Zadeh K, Gutekunst L, Mehrotra R, Kovesdy CP, Bross R, Shinaberger CS and Kopple JD, 2010. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. *Clinical Journal of the American Society of Nephrology*, 5, 519-530.
- Karlsson C, Obrant KJ and Karlsson M, 2001. Pregnancy and lactation confer reversible bone loss in humans. *Osteoporosis International*, 12, 828-834.
- Katai K, Miyamoto K, Kishida S, Segawa H, Nii T, Tanaka H, Tani Y, Arai H, Tatsumi S, Morita K, Taketani Y and Takeda E, 1999. Regulation of intestinal Na⁺-dependent phosphate co-transporters by a low-phosphate diet and 1,25-dihydroxyvitamin D₃. *Biochemical Journal*, 343, 705-712.
- Kemi VE, Karkkainen MU and Lamberg-Allardt CJ, 2006. High phosphorus intakes acutely and negatively affect Ca and bone metabolism in a dose-dependent manner in healthy young females. *British Journal of Nutrition*, 96, 545-552.
- Kemi VE, Karkkainen MU, Karp HJ, Laitinen KA and Lamberg-Allardt CJ, 2008. Increased calcium intake does not completely counteract the effects of increased phosphorus intake on bone: an acute dose-response study in healthy females. *British Journal of Nutrition*, 99, 832-839.
- Kemi VE, Karkkainen MU, Rita HJ, Laaksonen MM, Outila TA and Lamberg-Allardt CJ, 2010. Low calcium:phosphorus ratio in habitual diets affects serum parathyroid hormone concentration and calcium metabolism in healthy women with adequate calcium intake. *British Journal of Nutrition*, 103, 561-568.

- Kent GN, Price RI, Gutteridge DH, Smith M, Allen JR, Bhagat CI, Barnes MP, Hickling CJ, Retallack RW, Wilson SG, Rowena D, Roger IP, Margaret S, Chotoo IB, Charmian D and Andrew SJ, 1990. Human lactation: forearm trabecular bone loss, increased bone turnover, and renal conservation of calcium and inorganic phosphate with recovery of bone mass following weaning. *Journal of Bone and Mineral Research*, 5, 361-369.
- Kersting M and Clausen K, 2003. Ernährungsphysiologische Auswertung einer repräsentativen Verzehrsstudie bei Säuglingen und Kleinkindern VELS mit dem Instrumentarium der DONALD Studie. *Forschungsinstitut für Kinderernährung, Dortmund, Germany*, 103 pp.
- Kesse E, Boutron-Ruault MC, Norat T, Riboli E and Clavel-Chapelon F, 2005. Dietary calcium, phosphorus, vitamin D, dairy products and the risk of colorectal adenoma and cancer among French women of the E3N-EPIC prospective study. *International Journal of Cancer*, 117, 137-144.
- Kesse E, Bertrais S, Astorg P, Jaouen A, Arnault N, Galan P and Hercberg S, 2006. Dairy products, calcium and phosphorus intake, and the risk of prostate cancer: results of the French prospective SU.VI.MAX (Supplémentation en Vitamines et Minéraux Antioxydants) study. *British Journal of Nutrition*, 95, 539-545.
- Kido S, Kaneko I, Tatsumi S, Segawa H and Miyamoto K, 2013. Vitamin D and type II sodium-dependent phosphate cotransporters. *Contributions to Nephrology*, 180, 86-97.
- Kovacs CS, 2014. Bone development and mineral homeostasis in the fetus and neonate: Roles of the calciotropic and phosphotropic hormones. *Physiological Reviews*, 94, 1143-1218.
- Lakshmanan FL, Rao RB and Church JP, 1984. Calcium and phosphorus intakes, balances, and blood levels of adults consuming self-selected diets. *American Journal of Clinical Nutrition*, 40, 1368-1379.
- Lemann JJ, 1996. Calcium and phosphate metabolism: an overview in health and in calcium stone formers. In: *Kidney stones: medical and surgical management*. Eds Coe FL, Favus MJ, Pak CY, Parks JH and Preminger GM. *Lipincott-Raven Publishers, Philadelphia, PA, USA*, 259-288 pp.
- Lemons JA, Moye L, Hall D and Simmons M, 1982. Differences in the composition of preterm and term human milk during early lactation. *Pediatric Research*, 16, 113-117.
- Lutwak L, Laster L, Gitelman HJ, Fox M and Whedon GD, 1964. Effects of high dietary calcium and phosphorus on calcium, phosphorus, nitrogen and fat metabolism in children. *American Journal of Clinical Nutrition*, 14, 76-82.
- Mahalko JR, Sandstead HH, Johnson LK and Milne DB, 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *American Journal of Clinical Nutrition*, 37, 8-14.
- Marks J, Debnam ES and Unwin RJ, 2010. Phosphate homeostasis and the renal-gastrointestinal axis. *American Journal of Physiology*, 299, F285-F296.
- Marshall DH, Nordin BEC and Speed R, 1976. Calcium, phosphorus and magnesium requirement. *Proceedings of the Nutrition Society*, 35, 163-173.
- Martin AD, Bailey DA, McKay HA and Whiting S, 1997. Bone mineral and calcium accretion during puberty. *American Journal of Clinical Nutrition*, 66, 611-615.
- Mataix J, Aranda P, Lopez-Jurado M, Sanchez C, Planells E and Llopis J, 2006. Factors influencing the intake and plasma levels of calcium, phosphorus and magnesium in southern Spain. *European Journal of Nutrition*, 45, 349-354.
- Mataloun MM and Leone CR, 2000. Human milk mineral intake and serum concentrations of calcium and phosphorus in newborn term infants: influence of intrauterine growth restriction. *Acta Paediatrica*, 89, 1093-1097.
- McHardy GJR and Parsons DS, 1956. The absorption of inorganic phosphate from the small intestine of the rat. *Quarterly Journal of Experimental Physiology*, 41, 398-409.

- Mensink GB, Hesecker H, Richter A, Stahl A and Vohmann C (Robert Koch-Institut & Universität Paderborn), 2007. Forschungsbericht: Ernährungsstudie als KIGGS-Modul (EsKiMo). 143 pp.
- Mertz W, 1987. Use and misuse of balance studies. *Journal of Nutrition*, 117, 1811-1813.
- Michaud DS, Spiegelman D, Clinton SK, Rimm EB, Willett WC and Giovannucci E, 2000. Prospective study of dietary supplements, macronutrients, micronutrients, and risk of bladder cancer in US men. *American Journal of Epidemiology*, 152, 1145-1153.
- Mitchell DM and Jüppner H, 2010. Regulation of calcium homeostasis and bone metabolism in the fetus and neonate. *Current Opinion in Endocrinology, Diabetes and Obesity*, 17, 25-30.
- Moe SM, 2008. Disorders involving calcium, phosphorus, and magnesium. *Primary Care: Clinics in Office Practice*, 35, 215-237.
- Moe SM, Zidehsarai MP, Chambers MA, Jackman LA, Radcliffe JS, Trevino LL, Donahue SE and Asplin JR, 2011. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. *Clinical Journal of the American Society of Nephrology*, 6, 257-264.
- Moller UK, Vieth Streym S, Mosekilde L and Rejnmark L, 2012. Changes in bone mineral density and body composition during pregnancy and postpartum. A controlled cohort study. *Osteoporosis International*, 23, 1213-1223.
- Montalto MB and Benson JD, 1986. Nutrient intakes of older infants: effect of different milk feedings. *Journal of the American College of Nutrition*, 5, 331-341.
- Netherlands Food and Nutrition Council, 1992. Recommended dietary allowances 1989 in The Netherlands. The Hague, 115 pp.
- NHMRC (National Health and Medical Research Council), 2005. Nutrient Reference Values for Australia and New Zealand including recommended dietary intakes. 317 pp.
- Nickkho-Amiry M, Prentice A, Ledi F, Laskey MA, Das G, Berry JL and Mughal MZ, 2008. Maternal vitamin D status and breast milk concentrations of calcium and phosphorus. *Archives of Disease in Childhood*, 93, 179.
- Nishimuta M, Kodama N, Morikuni E, Yoshioka YH, Takeyama H, Yamada H, Kitajima H and Suzuki K, 2004. Balances of calcium, magnesium and phosphorus in Japanese young adults. *Journal of Nutritional Science and Vitaminology*, 50, 19-25.
- Nishimuta M, Kodama N, Shimada M, Yoshitake Y, Matsuzaki N and Morikuni E, 2012. Estimated equilibrated dietary intakes for nine minerals (Na, K, Ca, Mg, P, Fe, Zn, Cu, and Mn) adjusted by mineral balance medians in young Japanese females. *Journal of Nutritional Science and Vitaminology*, 58, 118-128.
- Nordic Council of Ministers, 2004. Nordic Nutrition Recommendations. Integrating nutrition and physical activity. 4th edition. 435 pp.
- Nordic Council of Ministers, 2014. Nordic Nutrition Recommendations 2012. Integrating nutrition and physical activity. 5th edition. 627 pp.
- Nordin BEC, 1989. Phosphorus. *Journal of Food & Nutrition*, 45, 62-75.
- NRC (National Research Council), 1953. Recommended Dietary Allowances. A Report of the Food and Nutrition Board, Publication 302. Washington, DC, USA.
- O'Brien KO, Kerstetter JE and Insogna KL, 2014. Phosphorus. In: *Modern Nutrition in Health and Disease*. Eds Ross AC, Caballero B, Cousins RJ, Tucker KL and Ziegler TR. Lippincott Williams & Wilkins, Philadelphia, PA, USA, 150-158.
- Oenning LL, Vogel J and Calvo MS, 1988. Accuracy of methods estimating calcium and phosphorus intake in daily diets. *Journal of the American Dietetic Association*, 88, 1076-1080.

- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS and Lutz R, 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Federation Proceedings*, 11, 775-783.
- Oliveira RB, Cancela AL, Gracioli FG, Dos Reis LM, Draibe SA, Cuppari L, Carvalho AB, Jorgetti V, Canziani ME and Moyses RM, 2010. Early control of PTH and FGF23 in normophosphatemic CKD patients: a new target in CKD-MBD therapy? *Clinical Journal of the American Society of Nephrology*, 5, 286-291.
- Paul AA, Black AE, Evans J, Cole TJ and Whitehead RG, 1988. Breastmilk intake and growth in infants from two to ten months. *Journal of Human Nutrition and Dietetics*, 1, 437-450.
- Penido MG and Alon US, 2012. Phosphate homeostasis and its role in bone health. *Pediatric Nephrology*, 27, 2039-2048.
- Pennington JA, 1994. *Bowes and Church's food values of portions commonly used*. JB Lippincott, Philadelphia, PA, USA, 480 pp.
- Pettifor JM, 2008. What's new in hypophosphataemic rickets? *European Journal of Pediatrics*, 167, 493-499.
- Pocock SJ, Ashby D, Shaper AG, Walker M and Broughton PM, 1989. Diurnal variations in serum biochemical and haematological measurements. *Journal of Clinical Pathology*, 42, 172-179.
- Portale AA, Halloran BP and Morris RC, Jr., 1987. Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *Journal of Clinical Investigation*, 80, 1147-1154.
- Prentice A and Bates CJ, 1994. Adequacy of dietary mineral supply for human bone growth and mineralisation. *European Journal of Clinical Nutrition*, 48 (Suppl 1), S161-176 discussion S177.
- Prentice A, 2003. Micronutrients and the bone mineral content of the mother, fetus and newborn. *Journal of Nutrition*, 133, 1693S-1699S.
- Prié D and Friedlander G, 2010. Genetic disorders of renal phosphate transport. *The New England Journal of Medicine*, 362, 2399-2409.
- Quarles LD, 2008. Endocrine functions of bone in mineral metabolism regulation. *The Journal of Clinical Investigation*, 118, 3820-3828.
- Ramasamy I, 2008. Inherited disorders of calcium homeostasis. *Clinica Chimica Acta*, 394, 22-41.
- Roberts PH, Kett CH and Ohlson MA, 1948. Nutritional status of older women; nitrogen, calcium phosphorus retentions of nine women. *Journal of the American Dietetic Association*, 24, 292-299.
- Roe MA, Bell S, Oseredczuk M, Christensen T, Westenbrink S, Pakkala H, Presser K and Finglas PM, 2013. Updated food composition database for nutrient intake. EFSA Supporting publication 2013:EN-355, 21 pp.
- Rowe JW, Andres R, Tobin JD, Norris AH and Shock NW, 1976. The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. *Journal of Gerontology*, 31, 155-163.
- RSC, 2004. Royal Society of Chemistry, Periodic Table website - phosphorus. Royal Society of Chemistry (RSC). Accessed on 30 June 2015. Available online: <http://www.rsc.org/periodic-table/element/15/phosphorus>
- Sabbagh Y, Giral H, Caldas Y, Levi M and Schiavi SC, 2011. Intestinal phosphate transport. *Advances in Chronic Kidney Disease*, 18, 85-90.
- Sann L, Bienvenu F, Lahet C, Bienvenu J and Bethenod M, 1981. Comparison of the composition of breast milk from mothers of term and preterm infants. *Acta Paediatrica Scandinavica*, 70, 115-116.
- SCF (Scientific Committee for Food), 1993. Nutrient and energy intakes for the European Community. Reports of the Scientific Committee for Food, 31st Series. Food - Science and Technique, European Commission, Luxembourg, 248 pp.

- Schaafsma G, 1981. The influence of dietary calcium and phosphorus on bone metabolism. PhD thesis. Wageningen, The Netherlands, 119 pp.
- Schiavi SC and Kumar R, 2004. The phosphatonin pathway: new insights in phosphate homeostasis. *Kidney International*, 65, 1-14.
- Scouler FI, Pace JK and Davis AN, 1957. The calcium, phosphorus and magnesium balances of young college women consuming self-selected diets. *Journal of Nutrition*, 62, 489-501.
- Segawa H, Kaneko I, Yamanala S, Ito M, Kuwahata M, Inoue Y, Kato S and Miyamoto K, 2004. Intestinal Na-P(i) cotransporter adaptation to dietary P(i) content in vitamin D receptor null mice. *American Journal of Physiology*, 287, F39-F47.
- Sette S, Le Donne C, Piccinelli R, Arcella D, Turrini A and Leclercq C, 2011. The third Italian National Food Consumption Survey, INRAN-SCAI 2005-06 - Part 1: Nutrient intakes in Italy. *Nutrition, Metabolism and Cardiovascular Diseases*, 21, 922-932.
- Shigematsu T, Negi S and Group CR, 2012. Combined therapy with lanthanum carbonate and calcium carbonate for hyperphosphatemia decreases serum FGF-23 level independently of calcium and PTH (COLC Study). *Nephrology, Dialysis, Transplantation*, 27, 1050-1054.
- Slemenda CW, Reister TK, Hui SL, Miller JZ, Christian JC and Johnston CC, Jr., 1994. Influences on skeletal mineralization in children and adolescents: evidence for varying effects of sexual maturation and physical activity. *Journal of Pediatrics*, 125, 201-207.
- Sowers M, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF and Hollis B, 1993. Changes in bone density with lactation. *Journal of American Medical Association*, 269, 3130-3135.
- Specker BL, Beck A, Kalkwarf H and Ho M, 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics*, 99, E12.
- Spencer H, Kramer L, Osis D and Norris C, 1978. Effect of phosphorus on the absorption of calcium and on the calcium balance in man. *Journal of Nutrition*, 108, 447-457.
- Spencer H, Kramer L and Osis D, 1984. Effect of calcium on phosphorus metabolism in man. *American Journal of Clinical Nutrition*, 40, 219-225.
- Spencer H, Fuller H, Norris C and Williams D, 1994. Effect of magnesium on the intestinal absorption of calcium in man. *Journal of the American College of Nutrition*, 13, 485-492.
- Stanbury SW, 1971. The phosphate ion in chronic renal failure. In: *Phosphate et metabolisme phosphocalcique*. Ed Hioco DJ. Sandoz Laboratories, Paris, France, 356 pp.
- Takeda E, Yamamoto H, Yamanaka-Okumura H and Taketani Y, 2012. Dietary phosphorus in bone health and quality of life. *Nutrition Reviews*, 70, 311-321.
- Teegarden D, Lyle RM, McCabe GP, McCabe LD, Proulx WR, Michon K, Knight AP, Johnston CC and Weaver CM, 1998. Dietary calcium, protein, and phosphorus are related to bone mineral density and content in young women. *American Journal of Clinical Nutrition*, 68, 749-754.
- Tenenhouse HS and Murer H, 2003. Disorders of renal tubular phosphate transport. *Journal of the American Society of Nephrology*, 14, 240-248.
- Tenenhouse HS, 2005. Regulation of phosphorus homeostasis by the type IIa Na/phosphate cotransporter. *Annual Review of Nutrition*, 25, 197-214.
- Tobias JH, Steer CD, Emmett PM, Tonkin RJ, Cooper C and Ness AR, 2005. Bone mass in childhood is related to maternal diet in pregnancy. *Osteoporosis International*, 16, 1731-1741.
- Tseng M, Breslow RA, Graubard BI and Ziegler RG, 2005. Dairy, calcium, and vitamin D intakes and prostate cancer risk in the National Health and Nutrition Examination Epidemiologic Follow-up Study cohort. *American Journal of Clinical Nutrition*, 81, 1147-1154.

- Tzaphlidou M and Zaichick V, 2002. Neutron activation analysis of calcium/phosphorus ratio in rib bone of healthy humans. *Applied Radiation and Isotopes*, 57, 779-783.
- van Rossum CTM, Fransen HP, Verkaik-Kloosterman J, Buurma-Rethans EJM and Ocké MC, 2011. Dutch National Food Consumption Survey 2007-2010: Diet of children and adults aged 7 to 69 years. RIVM Report number: 350050006/2011, National Institute for Public Health and the Environment, 143 pp.
- Walton J and Gray TK, 1979. Absorption of inorganic phosphate in the human small intestine. *Clinical Science*, 56, 407-412.
- WCRF/AICR (World Cancer Research Fund/American Institute for Cancer Research), 2007. Food, nutrition, physical activity and the prevention of cancer: a global perspective. 537 pp.
- Widdowson EM and Spray CM, 1951. Chemical development in utero. *Archives of Disease in Childhood*, 26, 205-214.
- Wilkinson R, 1976. Absorption of calcium, phosphorus, and magnesium. In: Calcium, phosphate and magnesium metabolism. Ed Nordin BEC. Churchill Livingstone, Edinburgh, UK, 36-112.
- Witczak A and Jarnuszewska A, 2011. [The content of selected mineral nutrients in infant and follow-on formulae available at retail stores in Szczecin]. *Roczniki Państwowego Zakładu Higieny*, 62, 257-262.
- Yamamoto KT, Robinson-Cohen C, de Oliveira MC, Kostina A, Nettleton JA, Ix JH, Nguyen H, Eng J, Lima JA, Siscovick DS, Weiss NS and Kestenbaum B, 2013. Dietary phosphorus is associated with greater left ventricular mass. *Kidney International*, 83, 707-714.
- Yamawaki N, Yamada M, Kan-no T, Kojima T, Kaneko T and Yonekubo A, 2005. Macronutrient, mineral and trace element composition of breast milk from Japanese women. *Journal of Trace Elements in Medicine and Biology*, 19, 171-181.
- Yin J, Dwyer T, Riley M, Cochrane J and Jones G, 2010. The association between maternal diet during pregnancy and bone mass of the children at age 16. *European Journal of Clinical Nutrition*, 64, 131-137.
- Young VR, 1986. Nutritional balance studies: indicators of human requirements or of adaptive mechanisms? *Journal of Nutrition*, 116, 700-703.
- Zaichick V and Tzaphlidou M, 2002. Determination of calcium, phosphorus, and the calcium/phosphorus ratio in cortical bone from the human femoral neck by neutron activation analysis. *Applied Radiation and Isotopes*, 56, 781-786.
- Zaichick V and Tzaphlidou M, 2003. Calcium and phosphorus concentrations and the calcium/phosphorus ratio in trabecular bone from the femoral neck of healthy humans as determined by neutron activation analysis. *Applied Radiation and Isotopes*, 58, 623-627.

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	Method	Days	Age (years)	Number of subjects						
						Infants < 1 year	Children 1–< 3 years	Children 3–< 10 years	Children 10–< 18 years	Adults 18–< 65 years	Adults 65–< 75 years	Adults ≥ 75 years
Finland/1	DIPP	2000–2010	Dietary record	3	< 1–6	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	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 record (web) ^(d)	4	18–80					1 430	295	72
UK/1	DNSIYC-2011	2011	Dietary record	4	0.3–1.5	1 369	1 314					
UK/2	NDNS Rolling Programme (Years 1–3)	2008–2011	Dietary record	4	1–94		185	651	666	1 266	166	139

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

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

(d): The Swedish dietary records were introduced through the internet.

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

Age class	Country	Survey	Intake expressed in mg/day					Intake 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	1 213	245	196	192	113	290
	Germany	VELS	174	699	682	396	1 018	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	1 310	663	207	207	127	290
	United Kingdom	NDNS Rolling Programme Years 1–3	107	973	974	570	1 461	107	198	201	130	262
3 to < 10 years	Finland	DIPP_2001_2009	381	1 173	1 176	695	1 633	381	200	202	135	259
	France	INCA2	239	1 033	1 000	618	1 468	239	167	161	117	241
	Germany	EsKiMo	426	1 151	1 126	751	1 645	426	151	149	110	192
	Germany	VELS	146	808	767	512	1 201	146	144	139	106	201
	Italy	INRAN_SCAI_2005_06	94	1 202	1 144	812	1 734	94	165	160	122	225
	Netherlands	DNFCS 2007–2010	231	1 146	1 107	689	1 700	231	133	133	86	184
	United Kingdom	NDNS Rolling Programme Years 1–3	326	1 076	1 052	673	1 558	326	171	168	121	240
10 to < 18 years	Finland	NWSSP07_08	136	1 601	1 537	980	2 459	136	196	190	126	275
	France	INCA2	449	1 243	1 210	745	1 828	449	159	155	116	213
	Germany	EsKiMo	197	1 225	1 169	792	1 826	197	151	148	107	204
	Italy	INRAN_SCAI_2005_06	108	1 494	1 405	944	2 244	108	152	148	123	193
	Netherlands	DNFCS 2007–2010	566	1 397	1 334	791	2 207	566	131	128	84	189
	United Kingdom	NDNS Rolling Programme Years 1–3	340	1 231	1 187	726	1 845	340	151	149	110	206
18 to < 65 years	Finland	FINDIET2012	585	1 614	1 548	793	2 640	585	174	172	117	242
	France	INCA2	936	1 403	1 372	801	2 103	936	161	158	120	212
	Ireland	NANS_2012	634	1 767	1 745	985	2 702	634	177	175	125	241
	Italy	INRAN_SCAI_2005_06	1068	1 378	1 334	820	2 089	1068	151	148	119	192
	Netherlands	DNFCS 2007–2010	1023	1 671	1 628	961	2 520	1023	149	146	100	211
	Sweden	Riksmaten 2010	623	1 692	1 651	961	2 583	623	173	172	127	227
	United Kingdom	NDNS Rolling Programme Years 1–3	560	1 448	1 411	810	2 223	560	166	163	115	228

Age class	Country	Survey	n ^(a)	Intake expressed in mg/day				n	Intake expressed in mg/MJ			
				Average	Median	P5	P95		Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	210	1 426	1 367	665	2 251	210	175	171	120	245
	France	INCA2	111	1 372	1 351	787	1 931	111	161	158	124	211
	Ireland	NANS_2012	72	1 652	1 638	854	2 683	72	189	189	133	265
	Italy	INRAN_SCAI_2005_06	133	1 311	1 315	791	1 945	133	150	149	117	193
	Netherlands	DNFCS 2007–2010	91	1 478	1 448	717	2 233	91	162	163	111	213
	Sweden	Riksmaten 2010	127	1 558	1 528	981	2 250	127	182	176	142	233
	United Kingdom	NDNS Rolling Programme Years 1–3	75	1 498	1 479	607	2 341	75	180	175	122	245
≥ 75 years	France	INCA2	40	1 280	1 173	(c)	(c)	40	165	162	(c)	(c)
	Ireland	NANS_2012	34	1 484	1 402	(c)	(c)	34	193	191	(c)	(c)
	Italy	INRAN_SCAI_2005_06	69	1 332	1 279	828	1 941	69	153	152	121	190
	Sweden	Riksmaten 2010	42	1 531	1 637	(c)	(c)	42	182	181	(c)	(c)
	United Kingdom	NDNS Rolling Programme Years 1–3	56	1 253	1 169	(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 des 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; VELLS, 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, 2011a) 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 intake in females in different surveys according to age classes and country

Age class	Country	Survey	Intake expressed in mg/day					Intake 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	604	75	125	128	80	173
	Italy	INRAN_SCAI_2005_06	7	447	509	(c)	(c)	7	145	151	(c)	(c)
	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	1 164	255	206	203	116	299
	Germany	VELS	174	641	645	357	932	174	149	146	102	207
	Italy	INRAN_SCAI_2005_06	16	890	846	(c)	(c)	16	196	189	(c)	(c)
	United Kingdom	DNSIYC_2011	651	815	802	419	1 266	651	205	208	123	285
	United Kingdom	NDNS Rolling Programme Years 1–3	78	863	856	499	1 224	78	192	190	132	254
3 to < 10 years	Finland	DIPP_2001_2009	369	1 086	1 068	699	1 551	369	206	206	149	269
	France	INCA2	243	925	901	625	1 274	243	167	162	122	228
	Germany	EsKiMo	409	1 056	1 032	667	1 536	409	156	155	113	200
	Germany	VELS	147	750	742	483	1 076	147	145	142	103	200
	Italy	INRAN_SCAI_2005_06	99	1 155	1 138	694	1 672	99	160	156	120	226
	Netherlands	DNFCS 2007–2010	216	1 080	1 033	642	1 693	216	133	132	84	192
	United Kingdom	NDNS Rolling Programme Years 1–3	325	991	980	587	1 458	325	166	165	120	222
	United Kingdom	NDNS Rolling Programme Years 1–3	325	991	980	587	1 458	325	166	165	120	222
10 to < 18 years	Finland	NWSSP07_08	170	1 264	1 255	691	2 045	170	192	192	127	255
	France	INCA2	524	992	983	574	1 460	524	158	153	115	214
	Germany	EsKiMo	196	1 148	1 130	729	1 633	196	155	151	110	207
	Italy	INRAN_SCAI_2005_06	139	1 226	1 217	813	1 836	139	154	152	117	205
	Latvia ^(d)	FC_PREGNANTWOMEN_2011	12	1 561	1 458	(c)	(c)	12	155	152	(c)	(c)
	Netherlands	DNFCS 2007–2010	576	1 167	1 138	674	1 716	576	133	134	82	189
	United Kingdom	NDNS Rolling Programme Years 1–3	326	990	977	573	1 525	326	147	143	105	205
	United Kingdom	NDNS Rolling Programme Years 1–3	326	990	977	573	1 525	326	147	143	105	205
18 to < 65 years	Finland	FINDIET2012	710	1 293	1 242	706	2 057	710	181	176	117	264
	France	INCA2	1 340	1 084	1 060	619	1 612	1340	169	163	122	235
	Ireland	NANS_2012	640	1 302	1 274	750	1 964	640	178	173	127	241
	Italy	INRAN_SCAI_2005_06	1 245	1 151	1 124	687	1 685	1245	157	154	120	206
	Latvia ^(d)	FC_PREGNANTWOMEN_2011	990	1 541	1 443	892	2 568	990	182	167	114	299
	Netherlands	DNFCS 2007–2010	1 034	1 279	1 241	729	1 967	1034	155	151	100	228
	Sweden	Riksmaten 2010	807	1 336	1 301	800	1 989	807	184	173	128	238
	United Kingdom	NDNS Rolling Programme Years 1–3	706	1 127	1 106	627	1 701	706	171	167	116	240
	United Kingdom	NDNS Rolling Programme Years 1–3	706	1 127	1 106	627	1 701	706	171	167	116	240

Age class	Country	Survey	n ^(a)	Intake expressed in mg/day				n	Intake expressed in mg/MJ			
				Average	Median	P5	P95		Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	203	1 153	1 140	644	1 690	203	187	187	124	258
	France	INCA2	153	1 050	1 034	557	1 487	153	170	163	127	233
	Ireland	NANS_2012	77	1 372	1 333	819	2 069	77	202	198	145	261
	Italy	INRAN_SCAI_2005_06	157	1 098	1 082	631	1 643	157	159	155	114	219
	Netherlands	DNFCS 2007–2010	82	1 181	1 148	640	1 720	82	163	159	111	237
	Sweden	Riksmaten 2010	168	1 310	1 272	781	1 972	168	188	188	148	237
	United Kingdom	NDNS Rolling Programme Years 1–3	91	1 145	1 144	714	1 618	91	191	185	139	264
≥ 75 years	France	INCA2	44	1 000	975	(c)	(c)	44	167	164	(c)	(c)
	Ireland	NANS_2012	43	1 294	1 275	(c)	(c)	43	207	200	(c)	(c)
	Italy	INRAN_SCAI_2005_06	159	1 075	1 080	623	1 490	159	161	155	117	218
	Sweden	Riksmaten 2010	30	1 330	1 316	(c)	(c)	30	189	189	(c)	(c)
	United Kingdom	NDNS Rolling Programme Years 1–3	83	1 162	1 139	728	1 596	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 des 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; VELLS, 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, 2011a) 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 percentage contribution of different food groups (FoodEx2 level 1) to phosphorus intake in males

Food groups	Age							
	< 1 year	1 to < 3 years	3 to < 10 years	10 to < 18 years	18 to < 65 years	65 to < 75 years	≥ 75 years	
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 phosphorus intake in the age and sex group considered.

Appendix E. Minimum and maximum percentage contribution of different food groups (FoodEx2 level 1) to phosphorus intake in females

Food groups	Age						
	< 1 year	1 to < 3 years	3 to < 10 years	10 to < 18 years	18 to < 65 years	65 to < 75 years	≥ 75 years
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 phosphorus intake in the age and sex group considered.

Appendix F. Calculations for deriving Adequate Intakes for phosphorus

The below calculations are based on the AI (for infants aged 7–11 months) and the PRIs (for all other ages) for calcium (EFSA NDA Panel, 2015), as well as on atomic masses for calcium of 40.08, and of 30.97 for phosphorus. A molar ratio of 1.4:1 to 1.9:1 was used (Sections 2.3.7 and 6.1).

Age	AI for calcium (mg/day)	PRI for calcium (mg/day)	Calculated value for phosphorus (mg/day) based on a ratio of 1.9:1	Calculated value for phosphorus (mg/day) based on a ratio of 1.4:1
7–11 months	280		114	155
1–3 years		450	183	248
4–10 years		800	325	442
11–17 years		1 150	468	635
Adults 18–24 years ^(a)		1 000	407	552
Adults ≥ 25 years ^(a)		950	386	524

AI, Adequate Intake; PRI, Population Reference Intake.

(a): Including pregnant and lactating women.

ABBREVIATIONS

1,25(OH) ₂ D	1,25-dihydroxy-vitamin D (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
BMC	bone mineral content
BMD	bone mineral density
cAMP	cyclic adenosine monophosphate
cGMP	cyclic guanosine monophosphate
COMA	Committee on Medical Aspects of Food Policy
CI	confidence interval
CV	coefficient of variation
CVD	cardiovascular disease
D-A-CH	Deutschland–Austria–Confoederatio Helvetica
DH	UK Department of Health
DIPP	Type 1 Diabetes Prediction and Prevention
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 des 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
NANS	National Adult Nutrition Survey
NaPi-IIa, NaPi-IIb, NaPi-IIc	sodium-dependent phosphate transporters
NDNS	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
RI	Recommended Intake
RNI	Reference Nutrient Intake
RR	relative risk
SCF	Scientific Committee for Food
SD	standard deviation
sFRP-4	secreted frizzled-related protein 4
SU.VI.MAX	SUplémentation en Vitamines et Minéraux Anti-oXydants
UL	Tolerable Upper Intake Level
VELS	Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln
WHO	World Health Organization