FERROUS AMMONIUM PHOSPHATE
Chemical and Technical Assessment (CTA)

Prepared by Dr. Madduri V. Rao, and reviewed by Dr. Yoko Kawamura

1. Summary

The seventy-first meeting of JECFA evaluated the safety of ferrous ammonium phosphate (FAP) for use as a nutrient in iron fortification of foods. This Chemical and Technical Assessment summarizes data and information on FAP submitted to JECFA by Nestec Ltd.[1], in a dossier dated December 2008.

FAP is intended for use as an alternative to currently permitted iron fortification compounds. The compound consists of a 1:1:1 molar ratio of iron (II), phosphate and ammonium with an iron loading of approximately 30% by weight. FAP is produced by combining iron powder, phosphoric acid and ammonia solution.

FAP is specifically designed for use as nutrient supplement in food systems in which maintenance of the organoleptic properties of the formulation is of particular concern (e.g. high in fat or polyphenols). The material is a stable source of iron when added to solid or liquid food products at neutral pH but is highly soluble at the low pH (2-3) conditions of the stomach where it will dissociate to the respective iron(II), phosphate and ammonium ions to become nutritionally available. The bioavailability of ferrous ammonium phosphate is comparable to ferrous sulfate, commonly used for food fortification.

It is intended for use in a wide range of general food categories at levels that provide between 15-30% typically of the recommended daily allowance (RDA) for iron. The exact products and use-levels will depend on the region and population group but will be consistent with current iron fortification programs.

2. Description

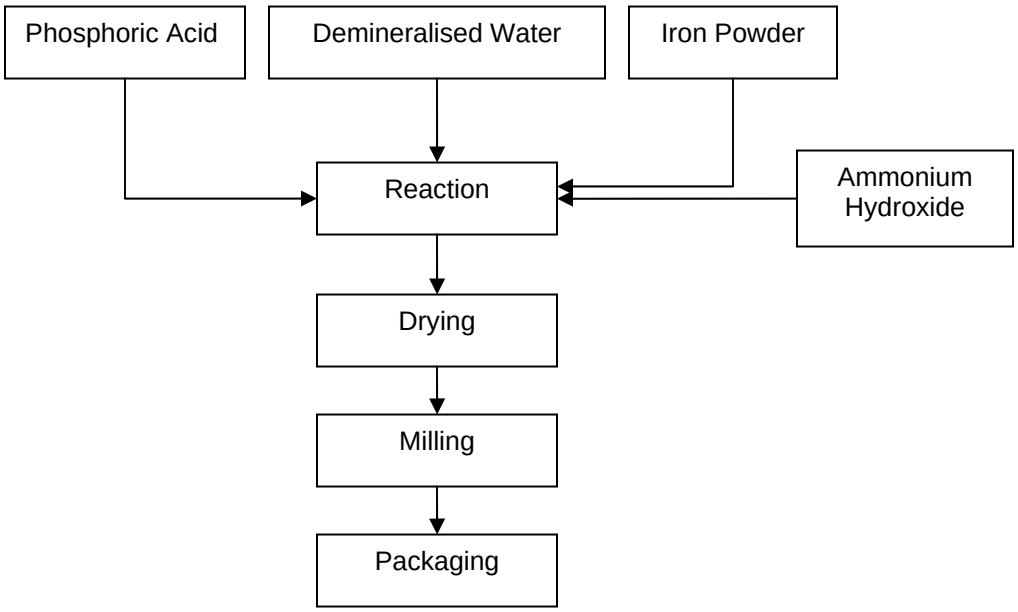
Ferrous ammonium phosphate (CAS No. 10101-60-7) is a greyish green powder and consists of a 1:1:1 molar ratio of iron(II), phosphate and ammonium with iron content ranging between 24 and 30% by weight..

3. Method of Manufacture

FAP is manufactured by mixing phosphoric acid, iron powder and ammonium hydroxide. Iron powder and phosphoric acid are combined in demineralised water with stirring to form a partial solution/suspension. The mixture is heated until no further hydrogen gas is evolved. Ammonia solution is added to the resultant slurry to yield the desired product, ferrous or iron(II) ammonium phosphate ($FeNH_4PO_4$). The product is then spray dried and milled to obtain a greyish green fine powder with the required particle size. Prior to packaging the material is purified by passing through a sieve and magnetic separation unit.

[1] Nestec Ltd., Corporate Regulatory & Scientific Affairs, Avenue Nestlé 55, CH-1800 Vevey Switzerland

Manufacturing Process of FAP



4. Characterization

4.1 Composition

FAP is a greyish-green coloured powder with an iron content ranging from 24-30% by weight. It is insoluble in water and soluble in dilute mineral acids. The pH of a 5% suspension in water is approximately 7. It is highly soluble at low pH (2-3), but poorly soluble at higher pH (7-12). The solubility product (K_{sp}) of FAP has been estimated to be 1.8×10^{-11} at pH 2 based on the concentration of free iron over time as determined by colorimetric methods. FAP dissociates to iron (II), ammonium, and phosphate ions in the acidic conditions prevailing in the stomach resulting in the bioavailability of iron (II).

4.2 Possible impurities (including degradation products)

Impurities such as iron (III), fluoride and heavy metals (lead, cadmium, arsenic and mercury) in the final product might come from the raw materials or as a consequence of the manufacturing process. During the manufacturing process, small amounts of iron (II) is oxidized to iron(III) resulting in about 5% of iron (III) in the final product as an impurity. The total iron (III) level permitted in the final product is restricted to no more than 7% in the specifications.

Based on the proposed fortification of products with FAP at levels delivering 15-30% of the Recommended Dietary Allowance (RDA) for iron (14 mg/day as defined by the European Union Directive 90/496/EEC is used for the purpose of this exposure analysis) and estimated daily intakes from all food categories, even the 97.5^{th} percentile of all-user consumption levels in female adults of 16.9 mg/person/day (equivalent to 3.7 to 5.1 mg of iron(II)) would result in a maximum intake of iron(III) of 1.2 mg/person/day from a batch at the limit of the specification (7%). The mean all-user consumption in male adults of 3.4 mg/person/day is a more realistic measure of the upper level of intake of ferrous ammonium phosphate and equates to a maximum exposure to iron(III) of 0.2 mg/person/day.

4.3 Rationale for proposed specifications

The proposed specifications include parameters to confirm the identity of the salt as a 1:1:1 molar ratio or iron(II), ammonium and phosphate ions and to restrict the presence of impurities such as iron (III), fluoride and heavy metals. The identity and purity parameters are consistent with JECFA specifications for other inorganic iron-containing salts, e.g. ferrous sulfate.

4.4 Analytical methods

The test methods are the standard methods published or referred to in the Combined Compendium of Food Additive Specifications (FAO JECFA Monographs 1, Volume 4, 2006) and the assay method is included in the specifications.

5. Functional uses

FAP is intended for use as a nutrient supplement for iron fortification. The choice of iron fortification compounds included in a food formulation is typically based on achieving the maximum bioavailability whilst not compromising the organoleptic properties of the final product to a significant degree. For example, ferrous salts such as iron sulfate and succinate have greater bioavailability than their ferric counterparts but at the same time they are highly soluble and react readily with components in the food product to cause discolouration, off-flavours, or rancidity. As a result, less soluble ferric alternatives such as ferric pyrophosphate or orthophosphate are commonly employed in products containing a high polyphenol or fat content in order to maintain the organoleptic properties of the formulation despite the concomitant reduction in iron bioavailability. Ferrous ammonium phosphate has been specifically developed for use as a fortificant in systems in which maintenance of the organoleptic properties of the food formulation is a particular concern. Ferrous ammonium phosphate is intended as a direct replacement for other permitted iron fortification compounds in food products containing polyphenols (cocoa, tea, etc.) or which have a high fat content.

5.1. Food categories and use levels

The intended use-levels and food categories for ferrous ammonium phosphate are summarized in Table 1. The general food categories are those of the food category system of the General Standard for Food Additives of the Codex Alimentarius Commission and the specific foods are subcategories of the general categories (FAO/WHO, 2009).

Table 1. Food categories and specific food uses

Food Category	Specific food uses
14.0 Beverages, excluding dairy products	14.1.4 Water-based flavoured drinks including "sport", "energy" or "electrolyte" drinks and particulated drinks: - Sport beverages
06.0 Cereals and cereal products	06.4.2 Dried pastas and noodles and like products - Instant noodles
05.0 Confectionary	05.1.1 Cocoa mixes (powders) and cocoa mass cake - Powdered drinking chocolate - Malt-based drinking powders
01.0 Dairy products and analogues	01.5 Milk powder and cream powder and powder analogues (plain): - Powdered milk beverages
13.0 Foodstuffs intended for Particular Nutritional Uses	13.3 Dietetic foods intended for special medical purpose (excluding products of food category 13.1) - Meal replacement bars
	13.4 Dietetic formulae for slimming purposes and weight reduction - Fortified cereal bars - Nutritionally complete supplement drinks, powdered and ready-to-drink
	13.5 Dietetic foods (e.g., supplementary foods for dietary use) excluding products of food categories 13.1-13.4 and 13.6
	13.6 Food supplements
12.0 Salts, spices, soups, sauces, salads, protein products and fermented soybean products	12.2.2 Seasonings and Condiments - Stock (seasoning) cubes and powders[1]
	12.2.2 Seasonings and Condiments - Instant noodles seasoning

[1]Bouillon/oxo or equivalent style products

The use levels of FAP in powdered chocolate beverages, powdered milk beverages, nutritionally complete supplement drinks (powdered and ready-to-drink), stock (seasoning) cubes/powders, and instant noodles are presented in Tables 2 and 3. The corresponding levels of iron, based on an iron content of 30% (consistent with a 1:1:1 w/w/w salt), are also presented in the Tables. The use-level for the remaining proposed food uses (sport beverages, fortified cereal bars, and meal replacement bars) provides 2.1 mg of iron per serving, which corresponds to 15% of the RDA for iron in adults in the EU, and 5.4 mg of iron per serving, which corresponds to 30% of the Daily Value (DV) for iron in the USA[2]. Variances in the intended use levels are based on current data submitted by the sponsor and reflect differing national regulations, cultures and nutritional requirements.

[2] The FDA reference daily intake value (RDI) of iron of 18 mg/person/day (U.S. FDA, 2008). Iron fortification salts are typically added as a percentage of the RDI, also referred to as the daily value (DV).

Table 2. Proposed foods uses and use levels for FAP and corresponding use levels of iron in the European Union

Food Category	Proposed Food-Use	Serving Size (g or ml)	Ferrous ammonium phosphate		Iron	
			Use-level (mg/ serving)	Use-level (mg/100 g or ml)	Use-level (mg/ serving)	Use-level (mg/100 g or ml)
14.0 Beverages, excluding dairy products	Sports beverages	250[a]	7	2.8	2.1	0.8
06.0 Cereals and cereal products	Instant noodles	30[b]	14	46.7	4.2	14
05.0 Confectionary	Powdered drinking chocolate	15[b]	13.6	90.7	4.1	27.2
	Malt-based drinking powders	15[b]	13.6	90.7	4.1	27.2
01.0 Dairy Products and Analogues	Powdered milk beverages	32.5[b] (Powder)	10.8	33.3	3.3	10
13.0 Foodstuffs intended for Particular Nutritional Uses	Fortified cereal bars	30[a]	7	23.3	2.1	7
	Meal replacement bars	60[c]	7	11.7	2.1	3.5
	Nutritionally complete supplement drinks, powdered and ready-to-drink	30[d] (Powder) 250[b] (RTD)	27.2	90.7 (Powder) 10.9 (RTD)	8.2	27.2 (Powder) 3.3 (RTD)
12.0 Salts, spices, soups, sauces, salads, protein products and fermented soybean products	Stock (seasoning) cubes and powders	2[b]	2.4[e]	120	0.7	36
	Instant noodles seasoning	30[b] (Noodles)[f]	14	46.7	4.2	14

RTD, Ready-to-Drink

[a] Provided by Nestec Ltd.

[b] FSA, 2002.

[c] http://www.muscle-shop.co.uk/meal-replacement-bars/ - Muscle Shop, 2006.

[d] CSFII (1994-1996), USDA, 1998.

[e] Fortification levels for stock cubes/powder reflect the use in the EU and these are currently slightly lower than use levels in the USA.

[f] As finished dried noodles product (fortification in either the noodles or the seasoning).

Table 3. Proposed foods uses and use levels for FAP and corresponding use levels of iron in the USA

Food Category	Proposed Food-Use	Serving Size [a] (g or ml)	Ferrous ammonium phosphate		Iron	
			Use-level (mg/ serving)	Use-level (mg/100 g or ml)	Use-level (mg/ serving)	Use-level (mg/100 g or ml)
14.0 Beverages, excluding dairy products	Sports beverages	240	18.0	7.5	5.4	2.25
06.0 Cereals and cereal products	Instant noodles	30[b]	14.0	46.7	4.2	14
05.0 Confectionary	Powdered drinking chocolate	15[b]	13.6	90.6	4.1	27.3
	Malt-based drinking powders	15[b]	13.6	90.6	4.1	27.3
01.0 Dairy Products and Analogues	Powdered milk beverages	32.5[b] (Powder)	10.9	33.5	3.3	10.1
13.0 Foodstuffs intended for Particular Nutritional Uses	Fortified cereal bars	40	18.0	45.0	5.4	13.5
	Meal replacement bars	40	18.0	45.0	5.4	13.5
	Nutritionally complete supplement drinks, powdered and ready-to-drink	240 (RTD)	18.0	7.50 (RTD)	5.4	2.23 (RTD)
12.0 Salts, spices, soups, sauces, salads, protein products and fermented soybean products	Stock (seasoning) cubes and powders	2[b]	10.9	545	3.3	10.1
	Instant noodles seasoning	30[b] (Noodles)[c]	14.0	46.7	4.2	14.0

RTD, Ready-to-Drink

[a] RACC = Reference Amount Customarily Consumed per Eating Occasion (Code of Federal Regulation 21 §101.12; U.S. Food and Drug Administration, 2008)

[b] Provided by Nestec Ltd.

[c] As finished dried noodles product (fortification in either the noodles or the seasoning)

6. Reactions and fate in foods

6.1 Determination of FAP levels in foods

The level of iron is used as a measure of the amount of FAP present in a fortified food product and can be determined either by colorimetry or atomic absorption spectrophotometry (AAS). Both

methods are well established and applicable to the range of foods that would typically be fortified with ferrous ammonium phosphate such as milk or cereal-based products.

6.2 Stability and degradation/reaction products

6.2.1 Food products with high polyphenol content

Addition of soluble iron salts to tea, chocolate milk or banana containing products may result in an interaction between the metal ion and iron sensitive components such as polyphenols in the food matrix. The resulting iron/phenol complex is an intense dark grey or black colour causing the product to become discoloured, particularly when a powdered beverage formulation is reconstituted with water or milk at high (boiling) temperatures. Experiments to evaluate discoloration both visually and by colorimetry have been performed in a range of beverages fortified with ferrous ammonium phosphate under typical formulation and reconstitution conditions and compared with controls containing either no supplemental iron salts or the common fortificant, ferrous sulfate (Sher, et al., 2001, Rekhif, et al., 2002, US Patents). In general, no colour changes were observed in tea, cocoa powders, or milk products under conditions typical of use. In the majority of cases, ferrous ammonium phosphate was more effective than ferrous sulfate at retaining product colour and was often comparable to the product without iron supplementation.

Addition of FAP to bouillon products (particularly shrimp or beef flavoured ones) resulted in general in less darkening or discoloration than addition of other iron salts such as ferrous fumarate, ferric pyrophosphate or ferric sodium ethylenediamine tetraacetic acid. The organoleptic properties were further improved by addition of soluble zinc compounds including zinc sulfate. When bouillon cubes fortified with irons salts were used for the preparation of foods containing high levels of polyphenols (e.g. aubergine stews), only those containing FAP did not have a detrimental effect on the colour of the final food matrix (Nestlé, 2006).

6.2.2 Food Products with High Fat Content

The addition of soluble iron sources to fat containing products, in particular products high in unsaturated fatty acids, can result in lipid oxidation and lead to changes in the flavour and nutritional quality of the product. Accelerated stability studies have been conducted with fish oils fortified with ferrous ammonium phosphate in order to mimic the potential effect of fortifying foods high in unsaturated fats (Sher *et al*., 2001; Rekhif *et al*., 2002). The time taken for the fish oil to undergo oxidation when fortified with ferrous ammonium phosphate was comparable to the control (without iron supplementation) and significantly slower than for oils fortified with ferrous sulfate. Unlike fish oils, food products will typically only contain a percentage of fat rather than being comprised entirely of fat.

6.2.3 Storage of FAP fortified products

Accelerated and real-time storage studies in cereals and a range of milk-based powders indicate that fortified with ferrous ammonium phosphate are stable over prolonged periods (representative of shelf-life) and that product quality is improved if exposure to air is minimized. Typically, the stability of products fortified with ferrous ammonium phosphate was comparable to those fortified with ferric pyrophosphate (Sher, et al., 2001).

7. References

FAO/WHO, 2009. Food category system. In: General Standards for Food Additives CODEX STAN 192-1995 (Rev. 10-2009), Annex B, pp. 9-48. Codex Alimentarius Commission, Joint Food Standards Program of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). Available at: http://www.codexalimentarius.net/web/standard_list.do?lang=en (Accessed 14 September 2009).

Council of the European Communities, 1990. Council Directive 90/496/EEC of 24 September 1990 on nutrition labelling for foodstuffs. Off. J. Eur. Communities, 33**,** L276, 40-44.

FAO, 2006. Combined compendium of food additive specifications. FAO JECFA Monographs, No. 1, Volume 4. Rome, Food and Agriculture Organization of the United Nations. Available at: http://www.fao.org/ag/agn/jecfa-additives/search.html?lang=en; http://www.fao.org/docrep/009/a0691e/a0691e00.HTM (Accessed 14 September 2009).

Food Standards Agency, 2002. Food Portion Sizes. 3rd Ed., Her Majesty's Stationery Office (HMSO), London, United Kingdom.

Muscle Shop, 2006. Meal Replacement Bars. Muscle Shop, with the Sports Nutrition Company Ltd., Easting Close, Worthing, United Kingdom. Available at: http://www.muscle-shop.co.uk/meal-replacement-bars/ (Accessed 15 September 2009).

Nestlé, 2006. Tasting Study: Chicken Bouillon Mass from Ivory Coast with Different Levels of Iron and Zinc Fortification *vs*. Non Fortification Mass. Unpublished study report for Project "Strength". Project Number RDSI 220007. Nestlé Product Technology Centre, Singen, Germany.

Rekhif, N., Sher, A., Vadehra, D.V., and Wedral, E.R., (inventors), 2002. Food Fortified with Iron (Assignee: Vevey, Switz., Nestec S.A.). U.S. Patent & Trademark Office, Washington, DC, USA, Patent No. 6,344.223 (Feb. 5, 2002). Available at: http://www.freepatentsonline.com/6344223.html (Accessed 14 September 2009).

European Scientific Committee on Food (SCF), 1993. Nutrient and Energy Intakes for the European Community, Opinion expressed on 11 December, 1992. Reports of the Scientific Committee for Food, 31st series, European Commission, Brussels, Belgium. Available at: http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_31.pdf (Accessed 15 September 2009).

European Scientific Committee on Food (SCF), 2003. Opinion of the Scientific Committee on Food on the Revision of Reference Values for Nutrition Labelling, expressed on 5 March 2003. Brussels, Belgium, European Commission, Brussels, Belgium. Available at: http://ec.europa.eu/food/fs/sc/scf/out171_en.pdf (Accessed 15 September 2009).

Sher, A., Vadehra, D.V., Wedral, E.R., and Rekhif, N., (inventors), 2001. Food Fortified with Iron (Applicant: Vevey, Switz., Societé des Produits Nestle .S.A.). Patent & Trademark Office, Washington DC, USA. World Intellectual Property Organization Patent No. WO 01/67897 A1 (Sep. 20, 2001). Available at: http://www.wipo.int/pctdb/en/wo.jsp?WO=2001%2F067897&IA=EP2001000619 (Accessed 14 September 2009),

U.S. FDA, 2008. Code of Federal Regulations (CFR), Title 21: Food and Drugs (U.S. Food and Drug Administration). Washington DC, USA. Available at: http://www.access.gpo.gov/cgi-bin/cfrassemble.cgi?title=200821 (Accessed 15 September 2009).

United States Department of Agriculture (USDA), 1998. Continuing Survey of Food Intakes by Individuals (CSFII) and Diet and Health Knowledge Survey (DHKS) 1994-1996. Prepared by the Agricultural Research Service, Beltsville Human Nutrition Research Center, Food Surveys Research Group Riverdale, MD, USA, PB98-500457, (CD-ROM).