EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 March 2013
EMA/HMPC/317318/2012
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Phaseolus vulgaris* L., fructus sine semine

Draft

The Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.

Braun H. Heilpflanzen – Lexikon für Ärzte und Apotheker, Anwendung, Wirkung und Toxicologie 4th ed. Gustav Fisher Verlag, Stuttgart, New York 1981, 162

Cerović A, Miletić I, Konić-Ristić A, Baralić I, Djordjević B, Djuricić I, Radusinovć M. The dry plant extract of common bean seed (*Phaseoli vulgari pericarpium*) does not have an effect on postprandial glycaemia in healthy human subject. *Bosn J Basic Med Sci* 2006, 6(3):28-33

Czech Pharmaceutical Codex. *Phaseoli fructus sine semine*. Český farmaceutický kodex Codex Pharmaceuticus Bohemicus. Editio prima, X-EGEM Publishers, Praha 1993

DAC, Deutscher Arzneimittel Codex. Phaseoli fructus sine semine. Deutscher Apotheker-Verlag, Stuttgart, 1986

Delfosse M. Drogues végétales et plantes médicinales. APB – service scientifique. 1998, 249

Dodoens R. Herbarius oft Cruydt-Boeck van Rembertus Dodonaeus. Plantijn –Moretus, Antwerpen 1608, 910

Hagers Handbuch der Pharmazeutischen Praxis (CDRom) 2012

Helmstädter A. Beans and diabetes: *Phaseolus vulgaris* preparations as antihyperglaycemic agents. *J Med Food* 2010, 13(2):251-254 [Epub 2010/02/06]

Martinez Alonso JC, Callejo Melgosa A, Fuentes Gonzalo MJ, Martin Garcia C. Angioedema induced by inhalation of vapours from cooked white bean in a child. *Allergol Immunopathol (Madr)* 2005, 33(4):228-30 [Epub 2005/07/28]

Meiss D. Reducing carbohydrate calories with bean extract. *Alternative and Complementary Therapies* 2004, 10(4):217-219

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8□00 **Facsimile** +44 (0)20 7523 7051
E-mail info@ema.europa.eu **Website** www.ema.europa.e□

An agency of the European Union

Neef H, Declercq P, Laekeman G. Hypoglycaemic activity of selected European plants. *Phytother Res* 1995, 9:45-48

Ocho-Anin Atchibri AL, Kouakou TH, Brou KD, Kouadio YJ, Gnakri D. Evaluation of bioactive components in seeds of *Phaseolus vulgaris* L. (Fabaceae) cultivated in Côte d'Ivoire. *J Appl Biosci* 2010, 31:1928-1934

Pari L, Venkateswaran S. Effect of an aqueous extract of *Phaseolus vulgaris* on plasma insulin and hepatic key enzymes of glucose metabolism in experimental animals. *Pharmazie* 2003, 58(12):916-919

Pari L, Venkateswaran S. Protective role of *Phaseolus vulgaris* on changes in the fatty acid composition in experimental diabetes. *J Med Food* 2004, 7(2):204-209 [Epub 2004/08/10]

Reuter H.D. Therapie mit Phytopharmaka (Pharmakologie – Indikationen Dosierungen) 1st ed. Gustav Fisher Verlag, Stuttgart, 1997, 153-154

Reynoso-Camacho R, Ramos-Gomez M, Loarca-Pina G. Advances in Agricultural and Food Biotechnology. Bioactive components in common beans (*Phaseolus vulgaris* L.), 2006, 217-236

Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycaemic effect of some edible plants. *J Ethnopharmacol* 1995, 48(1):25-32

Rougé P, Culerrier R, Thibau F, Didier A, Barre A. A case of severe anaphylaxis to kidney bean: phaseolin (vicilin) and PHA (lectin) identified as putative allergens. *Allergy* 2011, 66(2):301-302 [Epub 2010/09/02]

Van Hellemont J. Phytotherapeutisch compendium Algemene pharmaceutische bond 1985, 429-430

Verhelst G. Groot Handboek Geneeskrachtige Planten 4th ed. BVBA Mannavita, 2010, 427-428

Wichtl M. Teedrogen (Ein Handbuch für Apotheker und Ärzte). Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 1984, 81-82, 376

Wichtl M. Herbal Drugs and Phytopharmaceuticals. Medpharm GmbH Scientific Publishers, Stuttgart 1994, 373-374

References not supporting the assessment report

Arija I, Centeno C, Viveros A, Brenes A, Marzo F, Illera JC et al. Nutritional evaluation of raw and extruded kidney bean (*Phaseolus vulgaris* L. *var. pinto*) in chicken diets. *Poult Sci* 2006, 85(4):635-644 [Epub 2006/04/18]

Available at: http://www.phase2info.com/pdf/Phase2_Study10.pdf. Accessed 2012/03/07

Barrett ML, Udani JK. A proprietary alpha-amylase inhibitor from white bean (*Phaseolus vulgaris*): a review of clinical studies on weight loss and glycemic control. *Nutr J* 2011, 10:24

Carai MA, Fantini N, Loi B, Colombo G, Gessa GL, Riva A et al. Multiple cycles of repeated treatments with a *Phaseolus vulgaris* dry extract reduce food intake and body weight in obese rats. *Br J Nutr* 2011, 106(5):762-768 [Epub 2011/05/04]

Carai MAM, Fantini N, Loi B, Colombo G, Riva A, Morazzoni P. Potential efficacy of preparations derived from *Phaseolus vulgaris* in the control of appetite, energy intake, and carbohydrate metabolism. *Diabetes Metab Syndr Obes* 2009, 2:145-153

Carmalt J, Rosel K, Burns T, Janzen E. Suspected white kidney bean (*Phaseolus vulgaris*) toxicity in horses and cattle. *Aust Vet J.* 2003, 81(11):674-676 [Epub 2004/04/17]

Celleno L, Tolaini MV, D'Amore A, Perricone NV, Preuss HG. A Dietary supplement containing standardized *Phaseolus vulgaris* extract influences body composition of overweight men and women. *Int J Med Sci* 2007, 4(1):45-52

Chokshi D. Subchronic oral toxicity of a standardized white kidney bean (*Phaseolus vulgaris*) extract in rats. *Food Chem Toxicol* 2007, 45(1):32-40 [Epub 2006/10/19]

Chokshi D. Toxicity studies of Blockal™, a dietary supplement containing Phase 2 Starch Neutralizer (Phase 2), a standardized extract of the common white kidney bean (*Phaseolus vulgaris*). *Int J Toxicol* 2006, 25(5):361-371 [Epub 2006/08/31]

Dilawari JB, Kamath PS, Batta RP, Mukewar S, Raghavan S. Reduction of postprandial plasma glucose by Bengal gram dal (*Cicer arietinum*) and rajmah (*Phaseolus vulgaris*). *Am J Clin Nutr* 1981, 34(11):2450-2453 [Epub 1981/11/01]

Donatucci DA, Liener IE, Gross CJ. Binding of navy bean (*Phaseolus vulgaris*) lectin to the intestinal cells of the rat and its effect on the absorption of glucose. *J Nutr* 1987, 117(12):2154-2160 [Epub 1987/12/01]

Erner S, Meiss D. The Effect of TheraSlim™ (with Phase 2) on Weight, Body Composition, and Select Laboratory Parameters in Adults with Overweight and Mild-Moderate Obesity, 2003 Available at: http://www.phase2info.com/pdf/Phase2_Study8.pdf. Accessed 2012/03/07

Fantini N, Cabras C, Lobina C, Colombo G, Gessa GL, Riva A, et al. Reducing effect of a *Phaseolus vulgaris* dry extract on food intake, body weight, and glycemia in rats. *J Agric Food Chem* 2009, 57(19):9316-9323 [Epub 2009/09/08]

Grant G, Dorward PM, Buchan WC, Armour JC, Pusztai A. Consumption of diets containing raw soya beans (Glycine max), kidney beans (*Phaseolus vulgaris)*, cowpeas (*Vigna unguiculata*) or lupin seeds (*Lupinus angustifolius*) by rats for up to 700 days: effects on body composition and organ weights. *Br J Nutr* 1995, 73(1):17-29 [Epub 1995/01/01]

Harikumar KB, Jesil AM, Sabu MC, Kuttan R. A preliminary assessment of the acute and subchronic toxicity profile of phase2: an alpha-amylase inhibitor. *Int J Toxicol* 2005, 24(2):95-102 [Epub 2005/07/23]

Kik MJ, Huisman J, van der Poel AF, Mouwen JM. Pathologic changes of the small intestinal mucosa of pigs after feeding *Phaseolus vulgaris* beans. *Vet Pathol* 1990, 27(5):329-334 [Epub 1990/09/01]

Kilpatrick DC, Green C, Yap PL. Lectin content of slimming pills. *Br Med J (Clin Res Ed)* 1983, 286(6361):305 [Epub 1983/01/22]

Kluh I, Horn M, Hyblova J, Hubert J, Doleckova-Maresova L, Voburka Z et al. Inhibitory specificity and insecticidal selectivity of alpha-amylase inhibitor from *Phaseolus vulgaris*. *Phytochemistry* 2005, 66(1):31-39 [Epub 2005/01/15]

Koike T, Koizumi Y, Tang L, Takahara K, Saitou Y. The anti-obesity effect and the safety of taking "Phaseolamin™ 1600 diet". *Journal of New Remedies and Clinics (Japanese)* 2005, 54:1-16 [Japanese]

Lara-Diaz VJ, Gaytan-Ramos AA, Davalos-Balderas AJ, Santos-Guzman J, Mata-Cardenas BD, Vargas-Villarreal J et al. Microbiological and toxicological effects of Perla black bean (*Phaseolus vulgaris* L.) extracts: in vitro and in vivo studies. *Basic Clin Pharmacol Toxicol* 2009, 104(2):81-86

Martin-Cabrejas MA, Jaime L, Karanja C, Downie AJ, Parker ML, Lopez-Andreu FJ, et al. Modifications to physicochemical and nutritional properties of hard-to-cook beans (*Phaseolus vulgaris* L.) by extrusion cooking. *J Agric Food Chem* 1999, 47(3):1174-1182 [Epub 1999/12/20]

Marzo F, Alonso R, Urdaneta E, Arricibita FJ, Ibanez F. Nutritional quality of extruded kidney bean (*Phaseolus vulgaris* L. *var. pinto*) and its effects on growth and skeletal muscle nitrogen fractions in rats. *J Anim Sci* 2002, 80(4):875-879 [Epub 2002/05/11]

Marzolo MP, Amigo L, Nervi F. Hepatic production of very low density lipoprotein, catabolism of low density lipoprotein, biliary lipid secretion, and bile salt synthesis in rats fed a bean (*Phaseolus vulgaris*) diet. *J Lipid Res* 1993, 34(5):807-814 [Epub 1993/05/01]

Obiro WC, Zhang T, Jiang B. The nutraceutical role of the *Phaseolus vulgaris* alpha-amylase inhibitor. *Br J Nutr* 2008, 100(1):1-12 [Epub 2008/03/12]

Onakpoya I, Aldaas S, Terry R, Ernst E. The efficacy of *Phaseolus vulgaris* as a weight-loss supplement: A systematic review and meta-analysis of randomised clinical trials. *Br J Nutr* 2011, 106(2):196-202

Opala T, Rzymski P, Pischel I, Wilczak M, Wozniak J. Efficacy of 12 weeks supplementation of a botanical extract-based weight loss formula on body weight, body composition and blood chemistry in healthy, overweight subjects - A randomised double-blind placebo-controlled clinical trial. *Eur J Med Res* 2006, 11(8):343-350

Osorio L, Gamboa J. Random multicenter evaluation to test the efficacy of *Phaseolus vulgaris* (Precarb™) in obese and overweight individuals. Internal Report, 2005
Available at: http://www.phase2info.com/pdf/Phase2_Study10.pdf. Accessed 2012/03/07

Preuss HG. Bean amylase inhibitor and other carbohydrate absorption blockers: effects on diabesity and general health. *J Am Coll Nutr* 2009, 28(3):266-276 [Epub 2010/02/13]

Pusztai A, Grant G, Buchan WC, Bardocz S, de Carvalho AF, Ewen SW. Lipid accumulation in obese Zucker rats is reduced by inclusion of raw kidney bean (*Phaseolus vulgaris*) in the diet. Br J Nutr 1998, 79(2):213-221 [Epub 1998/04/16]

Pusztai A, Grant G, Duguid T, Brown DS, Peumans WJ, Van Damme EJ et al. Inhibition of starch digestion by alpha-amylase inhibitor reduces the efficiency of utilization of dietary proteins and lipids and retards the growth of rats. *J Nutr* 1995, 125(6):1554-1562 [Epub 1995/06/01]

Pusztai A, King TP, Clarke EM. Recent advances in the study of the nutritional toxicity of kidney bean (*Phaseolus vulgaris*) lectins in rats. *Toxicon* 1982, 20(1):195-197 [Epub 1982/01/01]

Reeves PG, Nielsen FH, Fahey GC Jr. AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-66A rodent diet. *J Nutr* 1993, 123(11): 1939-1951

Rondanelli M, Giacosa A, Orsini F, Opizzi A, Villani S. Appetite control and glycaemia reduction in overweight subjects treated with a combination of two highly standardized extracts from *Phaseolus vulgaris* and *Cynara scolymus*. *Phytother Res* 2011, 25(9):1275-82

Rothacker D. Reduction in body weight with a starch blocking diet aid: StarchAway™ comparison with placebo. *Leiner Health Products*, 2003. Available at: http://www.phase2info.com/pdf/Phase2_Study6.pdf. Accessed 2012/03/07

Santidrian S, de Moya CC, Grant G, Fruhbeck G, Urdaneta E, Garcia M, et al. Local (gut) and systemic metabolism of rats is altered by consumption of raw bean (*Phaseolus vulgaris* L. var *athropurpurea*). *Br J Nutr* 2003, 89(3):311-319 [Epub 2003/03/12]

Santimone M, Koukiekolo R, Moreau Y, Le Berre V, Rouge P, Marchis-Mouren G, et al. Porcine pancreatic alpha-amylase inhibition by the kidney bean (*Phaseolus vulgaris*) inhibitor (alpha-AI1) and structural changes in the alpha-amylase inhibitor complex. *Biochim Biophys Acta*. 2004, 1696(2):181-190 [Epub 2004/02/12]

Teguia A, Fru SF. The growth performances of broiler chickens as affected by diets containing common bean (*Phaseolus vulgaris*) treated by different methods. *Trop Anim Health Prod* 2007, 39(6):405-410 [Epub 2007/10/31]

Thom E. A randomized, double-blind, placebo-controlled trial of a new weight-reducing agent of natural origin. *J Int Med Res* 2000, 229-233

Tormo MA, Gil-Exojo I, Romero de Tejada A, Campillo JE. Hypoglycaemic and anorexigenic activities of an alpha-amylase inhibitor from white kidney beans (*Phaseolus vulgaris*) in Wistar rats. *Br J Nutr* 2004, 92(5):785-790 [Epub 2004/11/10]

Tormo MA, Gil-Exojo I, Romero de Tejada A, Campillo JE. White bean amylase inhibitor administered orally reduces glycaemia in type 2 diabetic rats. *Br J Nutr* 2006, 96(3):539-544 [Epub 2006/08/24]

Udani J, Hardy M, Madsen DC. Blocking carbohydrate absorption and weight loss: a clinical trial using Phase 2 brand proprietary fractionated white bean extract. *Altern Med Rev* 2004, 9(1):63-69 [Epub 2004/03/10]

Udani J, Singh BB. Blocking carbohydrate absorption and weight loss: a clinical trial using a proprietary fractionated white bean extract. *Altern Ther Health Med* 2007, 13(4):32-37 [Epub 2007/07/31]

Udani JK, Singh BB, Barrett ML, Preuss HG. Lowering the glycaemic index of white bread using a white bean extract. *Nutr J*. 2009, 8:52 [Epub 2009/10/29]

Vinson J, Al Kharrat H, Shuta D. Investigation of an amylase inhibitor on human glucose absorption after starch consumption. *The Open Nutraceuticals Journal* 2009, 2:88-91

Wu X, Xu X, Shen J, Perricone N, Preuss H. A dietary supplement containing standardized *Phaseolus vulgaris* extract influences body composition of overweight men and women. *Journal of Applied Research* 2010, 10:73-79

Yamada J, Yamamoto T, Yamaguchi T. Effects of combination of functional food materials on body weight, body fat percentage, serum triglyceride and blood glucose. 2007