Vitamin D (calciferol) comprises a group of fat-soluble seco-sterols. The major biologic function of vitamin D in humans is to maintain normal blood levels of calcium and phosphorus. Hence, the classic deficiency of the vitamin is related to bone formation, namely rickets in children and osteomalacia in adults. Recent research suggests that vitamin D plays a much broader disease-fighting role e.g. in muscular health, in diet-related chronic diseases, and in promoting immune health.

Currently, there are also scientific debates around other aspects of vitamin D, including the daily requirements, the appropriate methodology and cut-off for assessment of vitamin D status. Some reports of vitamin D insufficiency amongst various population groups have emerged, including amongst Malaysians.

ILSI SEAR Malaysia Country Committee organised this seminar to provide an update on the scientific understanding of vitamin D in human nutrition, including the various aspects mentioned above. The seminar provided a forum to discuss gaps in knowledge, especially in relation to Malaysians, and to enhance networking for future work on vitamin D. Held in Subang Jaya, Malaysia on 12 November 2013, the seminar was co-organised with the Nutrition Society of Malaysia, and was attended by 120 participants from various organisations including research institutions, academia, government agencies and the private sector. Mr. Geoffry Smith, President of ILSI Southeast Asia Region, delivered the welcome remarks for the seminar.

Update on Vitamin D in Human Nutrition

The seminar started off with *An Update on the Health Benefits of Vitamin D* by Professor Robin Daly of Deakin University, Melbourne, Australia. The principal actions of vitamin D are to regulate calcium and phosphate absorption in the gut, maintain calcium homeostasis via its interaction with parathyroid hormone and facilitate bone mineralisation. Severe vitamin D deficiency can lead to rickets in children and osteomalacia in adults, with mild deficiency also associated with secondary hyperparathyroidism, increased bone turnover and bone loss and impaired muscle function leading to an increased risk of falls and fractures. Recent evidence indicates that vitamin D treatment when combined with adequate dietary calcium can significantly reduce hip and vertebral fracture risk. However, scientific findings on the anti-fracture efficacy of vitamin D have been inconsistent. Prof. Daly also pointed out that emerging evidence suggests that caution is warranted about recommending high dose vitamin D supplementation for preventing falls and fractures. In recent years interest in the role of vitamin D has intensified due to increasing evidence that adequate vitamin D status has been associated with a decrease in the risk of a range of non-skeletal chronic diseases, including cardiovascular disease, hypertension, type 2 diabetes, certain types of cancer, autoimmune diseases, infectious diseases, some neurological and mental health conditions as well as all-cause and cardiovascular mortality. These benefits of vitamin D have been largely attributed to the identification of the vitamin D receptor in most tissues and cells of the body, and the observation that some extra-renal tissues also express the enzyme 1α-hydroxylase, which converts 25OHD to the biologically active metabolite 1,25-dihydroxyvitamin D, that regulates the expression of genes that can influence the biologic functions of various pathways linked to these diseases. Scientific support for these non-skeletal benefits have been derived mostly from animal studies while
evidence from human data is lacking. At present there are a number of large-scale RCTs underway evaluating the benefits of vitamin D, but these findings will not be known for several years. In the meantime, Prof. Daly felt that it is prudent that health professionals make appropriate recommendations with regard to dietary and supplemental vitamin D and sensible sun exposure to ensure that serum 25OHD concentrations are maintained at a level of at least 50 to 60 nmol/L year round.

After the discovery of vitamin D in the early 20th century and subsequent fortification activities, the bone deformities of rickets were drastically reduced, and this disease became uncommon in developed countries. However, recently there has been an upturn in cases of rickets and poor bone health in developed and developing countries. It has also been recognized that vitamin D status is lower than expected in many populations where sunshine is prevalent. In the second paper, Mr. Geoffry Smith, Essential Micronutrients Foundation, Singapore, summarised this Re-emergence of Vitamin D as a Public Health Concern. He traced the discovery of vitamin D and early approaches in treating deficiency of the vitamin. He summarised several aspects of vitamin D metabolism especially its role in rickets, osteoporosis and bone health. The past and current recommended intakes of the vitamin were summarised. Mr. Smith highlighted several studies on vitamin D status in Southeast Asia. Vitamin D fortification of food has been carried out in several countries, utilising different food vehicles. Several studies were highlighted to indicate the potential non-skeletal functions of vitamin D, including the relationship between Vitamin D status and cardiovascular disease mortality and incidence of some cancers. Lastly, he highlighted several research issues surrounding Vitamin D that require further attention.

In the third paper in this session, Ms. Fatimah Sulong, Food Safety and Quality Division, Ministry of Health Malaysia, provided a review of Regulatory Aspects of Vitamin D especially with regard to Malaysia. She provided an overview of existing regulations on voluntary micronutrient fortification, including some specific standards that require mandatory fortification for vitamin D in foods. Existing regulations on nutrition labelling and nutrition claims in relation to vitamin D were also presented. Vitamin D may be added to foods in accordance with Regulation 26 of the Food Regulations 1985. Under this regulation, food fortification is on a voluntary basis, governed by stipulated minimum level and maximum amount permitted daily for this nutrient. Regulations 18B stipulates the requirements for labelling of vitamin D (and other vitamins) in the nutrition information panel. Types of nutrient content claims and nutrient function claims and the associated conditions, including for vitamin D, are stipulated in Regulations 18C, 18D and 18E. Besides Malaysia, Ms. Fatimah also summarised the relevant regulations related to vitamin D fortification and claims in ASEAN and some developed countries. Some of these countries also have similar provisions in their legislations related to the addition and claims of vitamin D.

**Vitamin D Studies in Malaysia**

The first paper in this session of 5 presentations was presented by Prof. Poh Bee Koon, Universiti Kebangsaan Malaysia, who reported on Vitamin D Status of Malaysian Children Aged 4-12 years Old - Findings from the Four-Country South East Asian Nutrition Surveys (SEANUTS). A total of 856 children aged 4 to 12 years from selected kindergartens and primary schools in six regions of Malaysia were studied. The prevalence of vitamin D insufficiency and deficiency was 27.5% and 19.7%, respectively. Serum levels of vitamin D among boys was significantly higher (58.65 ± 1.46 nmol/L) compared with girls (48.95 ± 1.32 nmol/L) (p<0.001). This study also found that children living in urban areas had lower serum levels (52.83 ± 1.23 nmol/L) than their rural counterparts (58.14 ± 1.84 nmol/L) (p<0.05). On average, 64.6% of boys and 53.8% of girls spent more than 30 minutes per day doing outdoor activities under direct sunlight. Furthermore, 42.3% of girls wear scarves and long-sleeved shirts when doing outdoor activity, which reduces sun exposure. In conclusion, a high prevalence of vitamin D insufficiency was observed in Malaysian children, which suggests a need to put in place strategies that tackle vitamin D insufficiency among this population.

In the second presentation, Dr. Soma Mitra of the University of Nottingham Malaysia Campus shared with participants her study on Assessing Musculoskeletal Health in Malaysian School Children. In recent years, a new picture of the role of vitamin D in the functions of skeletal muscle is emerging. Dr. Mitra presented an overview of the study that is proposed to be conducted in school children between the ages 8 and 15 years. Grip-strength will be measured using a Hand grip dynamometer which has been widely demonstrated as a predictor of general muscular strength. Ultrasound measurements of bone will be taken on the same cohort to
evaluate patterns of bone mineral attenuation thereby screening for reduced bone health in the children. It is hoped to generate reference data and establish norms for Malaysian children on (a) grip strength and (b) bone ultrasound attenuation. In the future this research group also proposed to validate the above observations with serum 25 OH D (biomarker of Vitamin D) levels to establish surrogacy of muscle strength measurements and bone ultrasound measurements as clinical markers of Vitamin D status.

Dr. Hamid Jan, Universiti Sains Malaysia, presented the third paper on **Maternal Plasma and Breast Milk Vitamin D level from the USM Birth Cohort Study.** The study was carried out to assess maternal plasma and breast milk 25-hydroxyvitamin D (25(OH)D) concentrations and to determine the association between maternal plasma and breast milk 25 (OH) D levels. Data was obtained from the Universiti Sains Malaysia Birth Cohort Study, conducted from April 2010 to December 2012. The means of maternal plasma 25 (OH) D concentrations in the second and third trimesters of pregnancy were 48.40nmol/L and 59.10nmol/L, respectively. Most women (57%) had 25 (OH) D insufficiency in the second trimester and 4% had 25(OH) D deficiency. There were 60% women with normal plasma 25 (OH) D levels in the third trimester of pregnancy. All breast milk samples during the first year of postnatal life were shown with low levels of 25 (OH) D. No significant differences were detected among the breast milk 25 (OH) D concentrations from birth until 12 months of postnatal age. Increased maternal plasma 25 (OH) D concentration in the third trimester of pregnancy was associated with elevated level of breast milk 25 (OH) D at birth. The high prevalence of inadequate levels of maternal plasma and breast milk vitamin D might impose negative effects on maternal and children’s health. Strategies to improve vitamin D status among pregnant women are therefore warranted.

Dr. Mazliza Ramly, University of Malaya, shared with participants preliminary findings from the study entitled: **A randomized controlled trial of vitamin D supplements’ effect on cardiometabolic risks and quality of life among pre-menopausal women.** The study aimed to investigate whether vitamin D supplements can reduce the cardiometabolic risks and improve the quality of life among urban premenopausal women with vitamin D deficiency. A total of 192 pre-menopausal women age 30–55 years that were vitamin D deficient were recruited for this double blind, parallel, randomized controlled trial. They were randomized to receive either a vitamin D supplement (50,000 IU weekly for 8 weeks and 50,000 IU monthly for 10 months) (n=51) or placebo (n=59) for 12 months. To date, only 110 (57%) participants completed all study visits. Results obtained thus far showed that supplementation with vitamin D significantly increased serum total 25(OH)D at 6 and 12 months respectively. However, there were no significant differences between groups for all cardiometabolic risks as well as health related quality of life using SF-36v2. Dr. Mazliza concluded that improving vitamin D status through dietary supplementation in the short term (12 months) is unlikely to reduce cardiometabolic risks and health-related quality of life. Longitudinal studies may be required to establish the causality of vitamin D and cardiometabolic risks.

In the last paper in this series, Prof. Khor Geok Lin, International Medical University, Malaysia, presented an overview of **Studies on Vitamin D in Malaysia: Issues and Gaps.** A total of seven research studies conducted in the past decade in Malaysia that included data on vitamin D were reviewed. The objective of this review was to identify common issues of concern as well as to highlight information gaps to share with stakeholders. Two methodological issues that are of universal interest were addressed. Firstly, the use of different assay methods by different laboratories has raised worldwide concern on the accuracy of results. Some assay methods are reportedly not producing accurate estimates of total circulating 25OHD, and significant discrepancies of results between methods have also been reported. The second methodological issue is on the current practice of relying on a single cut-off point for vitamin D insufficiency. While there is increasing convergence on the level of less than 50nmol/L among researchers worldwide, others have argued for higher levels, which are more compatible with clinical outcomes. A major gap highlighted was the lack of accurate data on vitamin D content in foods and in dietary supplements. This information gap hampers the accurate assessment of dietary intake of vitamin D. Also lacking is a reliable measure of sun exposure that is feasible not only in research, but practicable as guidance for the general population. In light of the growing universal interests on the ubiquitous roles of vitamin D, efforts toward realising accurate assessment and viable guidelines for improving patient care and public health practice deserve full support.
Panel Discussion

The Seminar ended with a panel discussion focused on discussing several key issues related to vitamin D, especially in relation to Malaysia. The session was chaired by Prof. Khor Geok Lin and panel members comprised representatives from academia, scientific organisations and the private sector: Prof. Robin Daly, Mr. Geoffry Smith, Prof. Poh Bee Koon and Ms. Megawati Suzari of Fonterra Brands (M) Sdn Bhd. Seminar participants contributed actively to the discussions, which centred around highlighting the studies on vitamin D status of Malaysians, identifying the main research gaps and proposals for future activities and actions. It was noted that most studies have pointed out a high prevalence of vitamin D insufficiency among local population groups. Several major issues related to the topic include the different methods for determining vitamin D status, and the different cut-offs used by research groups to determine deficiency or insufficiency. These need to be resolved in order to have a more exact estimation of the population status of the vitamin. It was also highlighted that the lack of data on the vitamin D content of local foods has hampered dietary studies on intake of the vitamin. It was suggested that further meetings are required to discuss in greater detail the various issues highlighted. This will enable future directions for research and interventions to be mapped out.