University Alliance
Doctoral Training Alliance

DTA3/COFUND Programme Research Project Proforma

Page 1 – General Information

Project Code	TSAB07
Partner University	Teesside University
Faculty/School/Department/Research Centres	School of Health and Social Care
First supervisor Please provide name, email address (for UA use) and weblink	Prof V Zohoori v.zohoori@tees.ac.uk https://research.tees.ac.uk/en/persons/vida-zohoori
Second supervisor Please provide name, email address (for UA use) and weblink	Dr RM Duckworth ralphduckworth@talktalk.net Honorary Fellow, School of Health & Social Care, Teesside University, UK Formerly: Caries Science Area Leader for Unilever Oral Care Research Port Sunlight, UK
Third supervisor Please provide name, email address (for UA use) and weblink	Dr R McNaughton R.McNaughton@tees.ac.uk https://research.tees.ac.uk/en/persons/rebekah-mcnaughton-2
Fourth (external) supervisor	Prof S Levy Department of Preventive & Community Dentistry, The University of Iowa, US https://www. dentistry.uiowa.edu/steven-m-levy
External/industrial supervisor	
Which of the supervisors listed above is an early-career-researcher	Dr R McNaughton
Contact details for project for informal applicant queries	v.zohoori@tees.ac.uk
DTA Programme	DTA Applied Biosciences for Health
Project title	Predictor of fluorosis: total fluoride intake or subsequent fluoride absorption?

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 801604.

Page 2 – Project Description

Scientific Excellence (500 words)	Oral diseases are the most common non-communicable diseases (NCDs), which affect people throughout their lifetime, causing pain, discomfort, disfigurement and even death. According to the Global Burden of Disease Study 2016, almost half of the world's population are affected by oral diseases, with dental caries being assessed as the most prevalent condition. Due to the well-known role of fluoride in preventing dental caries, it has been added to water, salt, milk and dental products to reduce the prevalence of dental caries. Currently almost 380 million people worldwide in 25 countries receive fluoridated water at an optimal level of 0.7-1.0 ppm. However, excessive chronic fluoride exposure can result in undesirable dental fluorosis. It has been suggested that the fluoride intake should not exceed a tolerable upper intake level (UL) of 0.1 mg/kg body weight/day, especially during enamel formation, to minimise the risk of dental fluorosis. Excessive fluoride has also been linked with other adverse health effects such as musculoskeletal effects (bone fracture, irregular bone mass density and skeletal fluorosis), lower-IQ and neurological manifestations, thyroid disease (hypothyroidism), birth defects, bone cancer (osteosarcoma) and cardiovascular disease. Studies of fluoride and its adverse health outcomes have yielded somewhat conflicting results. These inconsistencies probably reflect differences in fluoride exposure or more importantly differences in fluoride metabolism. Several factors such as diet composition could alter the rate of fluoride bioavailability and therefore its absorption and consequent retention. Therefore, it is important to quantify the amount (percentage) of absorbed fluoride and body-retained fluoride rather than only the absolute total fluoride intake.
Aim (400 words)	Research rationale: To recommend and establish a dietary reference value (DRV) for any nutrient, it has been advocated to adjust this value (i.e., DRV) by "*factors to compensate for incomplete utilization and to encompass the variation both in the requirements among*

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	individuals and in the bioavailability among the food sources of the nutrient." Adequate intake (AI) and tolerable upper intake level (UL) values are the terminologies which have been considered and defined by several international organisations, such as the US Institute of Medicine (IoM), the European Food and Safety Authority (EFSA), and the Australian National Health and Medical Research Council (NHMRC), as guidelines to influence public health policy when adjusting fluoride intake. Scientific studies looking at the influence of fluoride intake on the risk of fluorosis should therefore include the rate of absorption into the risk model. One of the recommendations/conclusions of the "San Francisco Fluoride Symposium - 2017" was: "*The field of fluoride metabolism, focusing on overall fluoride bioavailability/absorption and fluoride biomarkers combined with clinical studies, merits new research initiatives to provide more evidence-based data to inform DRVs for fluoride.*" <u>Aims:</u> Due to the lack of relevant data, the aims of this project are to assess the bio/availability of fluoride from different sources; and its association with some health outcomes (e.g. development of dental fluorosis and bone mass density). <u>Methodology:</u> The project will: 1) measure availability of individual sources of fluoride by using *in vitro* digestion models after reconstructing several different diets in the lab; 2) estimate bioavailability of fluoride by using *in vivo* human model; and 3) investigate the overall association of bio/available fluoride with some health outcomes [e.g. development of dental fluorosis, bone mass density (BMD] using data from the Iowa fluoride study (IFS).
Strategic Relevance (300 words)	The currently suggested "optimal" intake of fluoride is based on limited scientific evidence. To assess the complex relationships among fluoride intakes, fluoride exposures, dental fluorosis, and dental caries, the longitudinal IFS recruited families with newborns during 1992 to 1995 from eight Iowa

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	hospital postpartum wards. Detailed questionnaires were sent every 1.5-6 months concerning water sources and fluoride exposures. Standardized dental exams were conducted at ages 5, 9, 13, 17 and 23(in progress). At about age 5, participants were invited to join the offshoot Iowa Bone Development Study. Bone densitometry assessments were conducted at ages 5, 8, 11, 13, 15, 17, 19 and 23(in progress). These included Dual-energy X-ray Absorptiometry (DXA) of hip, lumbar spine, and whole body from age 5; peripheral Quantitative Computed Tomography (pQCT) of the radius and tibia from age 11; and Multi-Detector Computed Tomography (MDCT) of the tibia from age 19. Physical activity and other factors were also assessed longitudinally. However, the IFS found an overlap among caries/fluorosis groups in mean fluoride intake and an extreme variability in individual fluoride intakes, which indicating that absolute F intake may not be the complete predictor of dental fluorosis prevalence. The IFS, therefore, is an ideal opportunity to assess the relationship between the rate of fluoride absorption from diet and toothpaste ingestion in children and clinical outcomes. This project sits within the School of Health and Social Care; and aligns with the current work being undertaken by staff, PhD and DTA students within the fluoride group, centring on the current important issues in fluoride research including fluoride measurement and total exposure for maximum dental benefit while minimising the risk of dental fluorosis, which is consistent with the WHO's current Priority Action Area - Oral Health and Fluorides.
Interdisciplinarity and fit with DTA3	The study comprises lab-based experiments and a human-model study with an extra advantage of having access to the data generated by a unique longitudinal cohort study (through the external supervisor – Prof S Levy who is the chief investigator of the IFS). This multi- and cross-disciplinary project, includes a wide range of disciplines such as nutrition, biology, biochemistry and dentistry.

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Industrial Relevance (300 words) Detail external placement opportunities or collaborations available as part of the project	Industry: Currently, food manufacturers do not need to label the fluoride content of their products. Due to the importance of avoiding excessive systemic fluoride intake, especially during 'tooth-vulnerable' periods, manufacturers should be encouraged to label the fluoride content of their products. The team has previously worked with industry; and the second supervisor (Dr RM Duckworth), in particular, has a long history of working with industry as well as securing funding from industry. The team will explore further opportunities for this project. Collaboration: The lead supervisor has a track record of collaborations with internationally recognised pioneers of fluoride metabolism and toxicity at different international institutes, in particular with Bauru Dental School/Brazil, Indiana University/US and University of Augusta/US. The team also works with the WHO on its current Priority Action Area - Oral Health and Fluorides. The student will have an opportunity to spend time with the overseas partner (Prof S Levy, Department of Preventive & Community Dentistry, The University of Iowa) to complete the third part of the project, and consequently to gain invaluable experience of collaborating in an international environment.
Economic and Societal Impact (300 words)	Dental caries still remains as the most globally prevalent chronic disease. Based on the World Health Organization (WHO) estimates, oral diseases are the fourth-most expensive diseases to treat in most industrialized countries. Effective use of fluorides for the prevention of dental caries has been highly recommended by the WHO. Due to the global extent of fluoridation schemes, particularly water fluoridation, the implementation of evidence-based recommendations for AI and UL for fluoride has been strongly praised. The results of the present study should provide primary evidence which may ultimately contribute to refining UL and consequently guiding public health policy- and decision-making for populations worldwide.

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Page 3 – Admission Requirements

Specific Admission Requirements Detail any subject specific degree qualifications or disciplines, relevant skills, experience	Applicants should hold or expect to obtain a good honours degree (2.1 or above) or Masters level qualification in nutrition, dentistry, biomedical sciences, biology, biochemistry, health or closely related discipline. The successful applicants will have a demonstrable understanding of laboratory analysis. Experience working with in vivo models would be advantageous.
Minimum IELTS score	

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