Institution: University of Aberdeen		
Unit of Assessment: 8 (Chemistry)		
Title of case study: Providing an evidence base for a maximum permissible level of inorganic arsenic in rice		
Period when the underpinning research was undertaken: 2008-2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Jörg Feldmann	Professor	06/2010-09/2020
Andy Meharg	Professor	09/1999-11/2012
Gareth Norton	Senior Lecturer	01/2005-current
Eva Krupp	Lecturer	10/2005-08/2020
Andrea Raab	Senior Research Fellow	01/2001-09/2020
Adam Price	Professor	03/1998-current
Period when the claimed impact occurred: 2013-2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact (indicative maximum 100 words)

The Trace Element Speciation Laboratory (TESLA), led by Professor Feldmann at the University of Aberdeen, have developed pioneering analytical chemistry techniques to quantify inorganic arsenic in rice and rice-based food. Feldmann's research has been key to raising awareness of the high levels of inorganic arsenic (iA) contained in rice, with his research forming the basis of a recommendation by the European Commission (EC) to formally establish a maximum permissible level of the class I carcinogen inorganic arsenic (in rice). Based on this recommendation, a maximum legal limit of 0.2 mg/kg (for adults) has since been identified by the Food and Agricultural Organisation (FAO) of the United Nations and the World Health Organisation (WHO). This was implemented into EU law in 2016.

Feldmann's research and technical expertise has also been key to facilitating low-cost methods for iA testing in the United States (U.S.) food industry and supporting reference material for baby food products in Canada. In order to help potential rice producers meet the 2016 EU standards, Feldmann developed two new affordable methods to low/medium income countries to detect levels of iA in their rice products. As a way to open up market opportunities he has worked closely with partners in Malawi to build capacity for iA testing while raising awareness of best practice amongst rice farmers in the country.

2. Underpinning research (indicative maximum 500 words)

Since the 1990s, the World Health Organisation (WHO), the European Union (EU), and the relevant authorities in the USA had established a maximum permissible level of inorganic arsenic in drinking water of 0.01 mg/l, however there was no such limit in foodstuffs. This is because arsenic in foodstuffs exhibits molecular forms with different toxicities: in its inorganic form, arsenic is highly toxic, whereas organoarsenicals are benign. Hence, introducing a legal limit was more complex than stating a simple arsenic concentration level permissible in food commodities.

This has presented a major challenge to introducing a legal limit in food products and has made it difficult for the EU to state a definitive permissible arsenic concentration level. In 2015, the European Commission (EC) recommended that member states provide speciated data on arsenic in food and monitor inorganic arsenic (iA), total arsenic (As) and other relevant arsenic species (Commission Recommendation (EU) 2015/1381). This generated a pressing need within the research community to establish a robust analytical method to determine levels of inorganic arsenic in rice and rice-based products. However, both a conventional method for detection of iA in rice and a universal maximum level (ML) for arsenic in foodstuffs had yet to be agreed.

Feldmann's group was the first to draw attention to the fact that in rice, the diversity of arsenic compounds is limited and a large proportion is in fact, iA. Furthermore, they demonstrated that rice represents one of the most highly arsenic-contaminated food commodities, specifically bran, husk, breakfast cereals and rice crackers [1] and as a staple ingredient of baby food products, rice presents a risk to babies and toddlers (due to their higher food intake per kg body weight) [2]. However, levels of iA had not been established due to a lack of techniques with sufficient sensitivity. By developing a straightforward analytical method combining high-performance liquid chromatography (HPLC) with inductively coupled plasma mass spectrometry (HPLC-ICP-MS; a combination of chromatography with element-specific detection), the TESLA research lab addressed this challenge, successfully detecting total arsenic, and for the first time iA content (combined arsenite and arsenate relative to total arsenic) [4]. This method was tested worldwide in a proficiency test organised by the EU [4]. Since the last REF period, the TESLA lab have been able to develop rice as reference material [P1] in which iA was certified for the first time (https://bit.ly/2NB7KeQ, see certification report, ERM-BC211)

In 2016, the European Commission (EC) introduced stricter standards for infants, 0.1 mg of inorganic arsenic per kg of food (0.1 mg/kg) compared to adults (0.2 mg/kg) for rice-based foods. This standard was not based on risk assessment and to date, EU legislation has had no effect on product violations (no lower iA concentrations have been measured in food destined for infants and young children than before the legislation was passed) (Signes-Pastor et al. 2017[1]).

The TESLA lab has worked to tackle this challenge by introducing a low-cost (and thereby more accessible) method, which would be suitable for use in the field and in turn ensure uptake of good practice within the wider scientific community. Whilst the established methodology, HPLC-ICPMS, has increased sample throughput in specialised labs [5], it is not suited for monitoring rice in the marketplace or in low-to-middle income countries, as it requires highly specialised equipment and relevant training (fewer than 30 labs worldwide have access to the equipment - none in Africa). Hence, Feldmann's initial research focussed on simplification of the analytical method by developing a technique targeting iA without chromatography by using selective volatilisation reactions [3]. This technique is different as it uses hydride generation (HG) ICP-MS (HG-ICP-MS) and has since been validated through direct comparison to the established methodology (HPLC-ICP-MS) for rice and rice-based products.

The HG method was confirmed to be sensitive, fast, and cheap and could be performed by any laboratory with an ICPMS or even an atomic absorption spectroscopy (AAS) instrument. The method also resulted in a shortening of sample measurement time and easier data treatment opening up the technique to non-specialists [5]. Whilst these developments bolstered the potential for analytical testing of rice to become more widespread [6], Feldmann cautioned in 2014 that given the impending EU regulation on iA concentration in rice, it was important that regulators do not prescribe a single standardised method, which would exclude new instrumental developments and potentially limit access to new markets.

Whilst the HPLC-ICP-MS methodology has expanded the range of researchers able to quantify iA in rice [4, 5], it was apparent that low-income countries still did not have the analytical means to do so. Marketed rice is not properly controlled due to the lack of affordable, rapid analysis. Moreover, baby food companies have been struggling to resource rice with low iA for their products since their traditional producers - in the EU - are located in areas with high arsenic levels. Hence, companies are looking for opportunities to source rice from producers outside of the EU. In order to facilitate sourcing of new rice markets in low-income countries, Feldmann developed a field-deployable method ('the Arsenator') based on a water testing kit, utilising selective volatilisation for iA (Gutzeit methodology) [7]. Following optimisation of the method, 30 rice commodities from the UK market were tested and compared to the reference method (HPLC-ICP-MS). In all but three rice samples, iA were determined, with no bias compared to the reference method, confirming its sensitivity [7]. This field-deployable method is projected to cost less than GBP3 per sample to run and has been field tested in Malawi [P2].

1 Signes-Pastor, A.J., et al 2017. Levels of infants' urinary arsenic metabolites related to formula feeding and weaning with rice products exceeding the EU inorganic arsenic standard. PLoS One, 12(5), p.e0176923.

3. References to the research (indicative maximum of six references)

References (citations via Scopus)

[1] Sun, G.X., Williams, P.N., Carey, A.M., Zhu, Y.G., Deacon, C., **Raab, A**., **Feldmann, J**., Islam, R.M. and **Meharg, A.A**., 2008. Inorganic arsenic in rice bran and its products are an order of magnitude higher than in bulk grain. *Environmental science & technology*, *42*(19), pp.7542-7546, doi: https://doi.org/10.1021/es801238p, 225 citations.

[2] **Meharg, A.A**., Sun, G., Williams, P.N., Adomako, E., Deacon, C., Zhu, Y.G., **Feldmann, J.** and **Raab, A**., 2008. Inorganic arsenic levels in baby rice are of concern. *Environmental Pollution*, *152*(3), pp.746-749, doi: https://doi.org/10.1016/j.envpol.2008.01.043, 143 citations.

[3] Musil, S., Pétursdóttir, Á.H., Raab, A., Gunnlaugsdóttir, H., **Krupp, E**. and **Feldmann, J**., 2014. Speciation without chromatography using selective hydride generation: inorganic arsenic in rice and samples of marine origin. *Analytical chemistry*, *86*(2), pp.993-999, doi: https://doi.org/10.1021/ac403438c, 73 citations.

[4] Petursdottir, A.H., Sloth, J.J. and **Feldmann, J**., 2015. Introduction of regulations for arsenic in feed and food with emphasis on inorganic arsenic, and implications for analytical chemistry. *Analytical and bioanalytical chemistry*, *407*(28), pp.8385-8396, doi: https://doi.org/10.1007/s00216-015-9019-1, 39 citations.

[5] Narukawa, T., Chiba, K., Sinaviwat, S. and **Feldmann, J**., 2017. A rapid monitoring method for inorganic arsenic in rice flour using reversed phase-high performance liquid chromatography-inductively coupled plasma mass spectrometry. *Journal of Chromatography A*, *1479*, pp.129-136, doi: https://doi.org/10.1016/j.chroma.2016.12.001, 21 citations.

[6] Pétursdóttir, Á.H., Friedrich, N., Musil, S., **Raab, A**., Gunnlaugsdóttir, H., **Krupp, E.M**. and **Feldmann, J**., 2014. Hydride generation ICP-MS as a simple method for determination of inorganic arsenic in rice for routine biomonitoring. *Analytical Methods*, *6*(14), pp.5392-5396, doi: https://doi.org/10.1039/c4ay00423j, 33 citations.

[7] Bralatei, E., Lacan, S., **Krupp, E.M**. and **Feldmann, J**., 2015. Detection of inorganic arsenic in rice using a field test kit: a screening method. *Analytical chemistry*, *87*(22), pp.11271-11276, doi: https://doi.org/10.1021/acs.analchem.5b02386, 32 citations.

[8] Gajdosechova, Z., Grinberg, P., Nadeau, K. Yang L., Meija J., Gurleyuk H., Wozniak B., **Feldmann, J** *et al.* CRM rapid response approach for the certification of arsenic species and toxic trace elements in baby cereal coarse rice flour certified reference material BARI-1. Anal Bioanal Chem 412, 4363–4373 (2020), doi: https://doi.org/10.1007/s00216-020-02673-x, 1 citation.

Grants:

[P1] **Feldmann, J** Stability tests ERM-BC211 sample preparation and measurements for total arsenic, arsenite and arsenate and dimethylarsenic acid, European Commission; 11/10-05/11; (GBP4,300)

[P2] **Feldmann, J** Field testing in Malawi, GCRF, Scottish Funding Council (internal pump priming); 2018; (GBP5000).

4. Details of the impact (indicative maximum 750 words)

The impact resulting from the research on arsenic in rice involves:

1) Providing an evidence base to inform maximum limits on iA around the world;
2) Reducing the cost of iA testing in the U.S. food industry;
3) Development of a certified reference material (CRM) for infant food matrices in Canada;
4) Building capacity for iA monitoring in Malawi;
5) Engaging with local rice farmers in Malawi – creating the infrastructure for field-testing.

1) Providing an evidence base to inform maximum limits on iA around the world

The large body of evidence [1-6] collated by Feldmann, Meharg and the wider TESLA lab, provided a sufficiently compelling argument for the Codex Committee (responsible for the preparation of draft standards to the European Commission) to meet to discuss introducing a maximum permissible limit for iA in rice. As a result, the FAO/WHO committee on contaminants in food hosted a debate in 2015 and the Codex Committee proposed a draft code of practice for the prevention and reduction of arsenic contamination in rice. Since the submission of this draft code (an advisory report), the committee has set the maximum permissible level of iA in polished rice at 0.2 mg/kg (FAO/WHO 2015). During their discussions, whilst no consensus on a maximum limit (ML) was reached for husked rice. Aberdeen research brought to the fore examination of the inextricable links inhibiting a global ML. This is confirmed by supplementary details of the advisory report (codex report B), which states that "…*divergent views were expressed as to what the ML for husked rice should be in terms of protection of human health while not having a negative impact on international trade*" [S1].

The European Commission introduced a maximum limit for four categories of rice in 2015, recognising that bran and husked rice have generally higher levels of iA (0.2 mg/kg for polished white rice, 0.25 mg/kg for parboiled and husked rice, and 0.3 mg/kg for rice crackers and waffles). However, rice used in the production of food for infants and young children was given a lower iA limit (0.1 mg/kg) [S2]. The setting of different maximum limits acknowledges the Aberdeen group's work [1], which identified and raised awareness of the relatively high levels of iA in bran, husk, breakfast cereals and rice crackers and the problem of babies eating rice-based products [2].

2) Reducing the cost of iA testing in the U.S. food industry

Research led by Feldmann and the TESLA lab led to development of cheaper methods for measuring iA in rice, including the HG-ICP-MS system. In the U.S., limits on iA in rice products mean that samples must be analysed to ensure compliance. Reported methods tend to use measurement of all species of As present in rice and other foods, which incurs high costs for the supplier, requiring trained staff and expensive equipment, and a high cost per sample (USD200). In March 2016, the Senior Research Agronomist at the U.S. Department of Agriculture (USDA) invited Feldmann and the TESLA lab to participate in an inter-laboratory evaluation of a simpler method for measuring iA [S3i]. The aim of this evaluation was to provide industry with a reliable and less expensive method to identify the levels of iA, (rather than full As speciation), in order to comply with market limits [S3ii]. In their final report, the USDA, as organiser of this trial, concluded that iA in rice can be measured with similar accuracy by the new HG-ICP-MS method developed by Feldmann (Pettursdottir et al. 2014 [6]) as the previously established more expensive HPLC-ICP-MS method with only minor differences. The HG-ICP-MS method was deemed to be simpler and faster, required less-expensive instrumentation and was able to be conducted by less-experienced staff [S4].

3) Development of a certified reference material (CRM) for infant food matrices in Canada

As of June 2019, Health Canada, a federal institution and part of the Health Portfolio (Public Health Agency of Canada, the Canadian Institutes of Health Research, the Patented Medicine Prices Review Board and the Canadian Food Inspection Agency), legislated MLs of iA in white and brown rice to 0.2 mg/kg and 0.35 m/kg, respectively. The National Research Council of Canada created a new certified reference material (CRM) rapid response approach, to 'fast track' the assessment of reference materials. To achieve this Health Canada brought together a team of 4-5 intentional labs worldwide with expertise in toxicity assessment and As speciation, including Feldmann [8]. This resulted in the development of the new CRM (BARI-1), which could be used to assess the accuracy of developed analytical methods for As speciation in infants' food. Principal Research Officer of the National Resource Council of Canada confirmed the value of Feldmann's contribution in a testimonial, stating '*BARI-1 will serve the world-wide science and regulatory community for decades to come. Your contribution from the early planning stages and the actual provision of measurement data on this CRM has been crucial to the success of this project'* [S5].

4) Building capacity for iA monitoring in Malawi

With regards to identifying products which meet the low limit of iA required in rice for infants and young children, food companies are searching for new areas from which to secure product, since the traditional regions (Italy, France, Spain, the US, India and China) produce rice with iA levels over the maximum limit of 0.1 mg/kg. This project [P2] represented the first step towards identifying and enabling a market beyond traditional regions, facilitated by EU regulation and uptake of the "Arsenator" field deployable method, which has enabled surveying of rice in low-income countries. In order to increase awareness of the value of screening rice in Malawi and to identify potential market opportunities, a workshop was organised for the Malawi regional agricultural advisors for rice schemes in July 2019. The main workshop, convened in Salima was attended by a total of fifty-five participants, including district development division manager, thirty-six rice farmers, thirteen field workers (agriculture extension development officers; AEDOs) and four area field supervisors (agriculture extension planning area – EPA – agriculture extension development coordinators – AEDCs) from various districts across the country. A further two were experts from the Lifuwu Research Institute [S6].

5) Engaging with local rice farmers in Malawi – creating the infrastructure for field testing

Prior to this workshop, smallholder farmers from Malawi were unaware of the toxic substances in rice. Following a demonstration of the field kit, farmers completed a questionnaire [S6], which demonstrated better understanding of what would constitute 'high quality' rice by EU buyers and a willingness to screen rice. The workshop provided a forum to discuss the use of a Farmer's cooperatives rice market where EU buyers could buy high quality rice directly from farmers rather than through venders who may exploit them. Farmers were able to ask the Ministry of Agriculture to speed up availability of screening facilities in the districts allowing farmers to access such screening services without difficulties [S6, S7]. Upon receiving training on how the field deployable method works, the majority of the AEDOs showed willingness to work with farmers in screening rice with elevated iA and offered to conduct the analyses on-site within their stations at their regional or district offices [S7]. A total of 87 student trainees (AEDOs) from the NRC and 13 academic staff members (lecturers and technicians) were trained, embedding good practices. Training modules have been established in ten secondary schools and screening services have been provided through Lilongwe University of Agriculture and Natural Resources [S7].

5. Sources to corroborate the impact (indicative maximum of 10 references)

[S1] FAO/WHO (2015): Joint FAO/WHO food standards programme codex committee on contaminants in foods. CX/CF 15/9/8 January 2015. Proposed draft code of practice for the prevention and reduction of arsenic contamination in rice.

[S2] EC 2015: Commission regulation (EU) 2015/1006 amending Regulation (EC) No 1881/2006 in regards to maximum levels of inorganic arsenic in foodstuffs (25 June 2015). Official Journal of the European Union.

[S3 (group)] (i) R.L. Chaney & S.J. Lehotay, USDA invitation letter to participate in inter-laboratory evaluation of a simpler method for measurement of inorganic As (*i*As) in powdered rice grain (March 2016); (ii) R.L. Chaney, C.E. Green, S.J. Lehotay, M. Bukowski (2016) Simpler Less Expensive Method for Analysis of inorganic As (iAs) in rice, USDA report and https://www.ars.usda.gov/research/publications/publication/?seqNo115=333695

[S4] FDA Arsenic in Rice and Rice products – Risk Assessment Report, p241. (2016) https://www.fda.gov/files/food/published/Arsenic-in-Rice-and-Rice-Products-Risk-Assessment-Report-PDF.pdf

[S5] Testimonial from the Principal Research Officer, National Resource Council, Canada.

[S6] A.T. Mlangeni & J. Feldmann, Report on the workshop promoting use of the field deployable method for screening rice with low inorganic arsenic content for baby food production among smallholder farmers in Malawi (2019).

[S7] Testimonial from Lilongwe University of Agriculture and Natural Resources.