Mr Christian James
TEC Partnership (Grimsby Institute of Further & Higher Education; GIFHE)
Grimsby
DN34 5BQ

Date: 26th October 2020

Supply of FS307036 - Assessing the impact of heat treatment on AMR genes

Following your tender/ proposal for the supply of **Assessing the impact of heat treatment on AMR genes** to Food Standards Agency (FSA), we are pleased confirm our intention to award this contract to you.

The attached contract details ("**Order Form**"), contract conditions and the **Annexes** set out the terms of the contract between FSA and TEC Partnership (Grimsby Institute of Further & Higher Education, GIFHE) for the provision of the deliverables set out in the Order Form.

We thank you for your co-operation to date and look forward to forging a successful working relationship resulting in a smooth and successful delivery of the deliverables. Please confirm your acceptance of the Conditions by signing and returning the Order Form within **7** days from the date of this Order Form.

We will then arrange for Order Form to be countersigned which will create a binding contract between us.

Yours faithfully,

Mark Croft

Procurement Category Manager

Order Form

1. Contract Reference	**FS307036**	
2. Date	26/10/2020	
3. Buyer	Food Standards Agency, Foss House, Peasholme Green, York, YO1 1PR	
4. Supplier	TEC Partnership, Grimsby Institute of Further & Higher Education (GIFHE), Nuns Corner, Grimsby, North East Lincolnshire, DN34 5BQ	
5. The Contract	The Supplier shall supply the deliverables described below on the terms set out in this Order Form and the attached contract conditions ("**Conditions**") and any **Annexes**. Unless the context otherwise requires, capitalised expressions used in this Order Form have the same meanings as in Conditions. In the event of any conflict between this Order Form and the Conditions, this Order Form shall prevail. Please do not attach any Supplier terms and conditions to this Order Form as they will not be accepted by the Buyer and may delay conclusion of the Contract.	
6. Deliverables	**Services**	See **Annex 3 – Supplier's Technical Proposal**
7. Specification	See **Annex 2 – Buyers Specification**	
8. Term	The Term shall commence on 1st November 2020 and the Expiry Date shall be 31st May 2021, unless it is otherwise extended or terminated in accordance with the terms and conditions of the Contract. The Buyer may extend the Contract for a period of up to 6 months by giving not less than 10 Working Days' notice in writing to the Supplier prior to the Expiry Date. The terms and conditions of the Contract shall apply throughout any such extended period.	

9. Charges	The Charges for the Deliverables shall be as set out in **Annex 4 - Supplier's Financial Proposal.**
10. Payment	All invoices must be sent, quoting a valid purchase order number (PO Number), to: Accounts-Payable.fsa@gov.sscl.com. Within **10** Working Days of receipt of your countersigned copy of this letter, we will send you a unique PO Number. You must be in receipt of a valid PO Number before submitting an invoice. To avoid delay in payment it is important that the invoice is compliant and that it includes a valid PO Number, PO Number item number (if applicable) and the details (name and telephone number) of your Buyer contact (i.e. Contract Manager). Non-compliant invoices will be sent back to you, which may lead to a delay in payment.
11. Buyer Authorised Representative	For general liaison your contact will continue to be [redacted] [redacted]
12. Address for notices	**Buyer:** FSA Procurement Foss House Peasholme Green York YO1 1PR **Supplier:** [redacted]

13. Key Personnel	See **Annex 3 – Supplier's Technical Proposal**
14. Procedures and Policies	The Buyer may require the Supplier to ensure that any person employed in the delivery of the Deliverables has undertaken a Disclosure and Barring Service check. The Supplier shall ensure that no person who discloses that he/she has a conviction that is relevant to the nature of the Contract, relevant to the work of the Buyer, or is of a type otherwise advised by the Buyer (each such conviction a "**Relevant Conviction**"), or is found by the Supplier to have a Relevant Conviction (whether as a result of a police check, a Disclosure and Barring Service check or otherwise) is employed or engaged in the provision of any part of the Deliverables.

Signed for and on behalf of the **Supplier**	Signed for and on behalf of the **Buyer**
Name: Christian James Job Title: Senior Research Fellow	Name: Mark Croft Job Title: Procurement Category Manager
Date: 28th October 2020	Date: 29th October 2020
Signature: [redacted]	Signature: [redacted]

Annex 1 – Authorised Processing Template

Contract:	FS307036 - Assessing the impact of heat treatment on AMR genes
Date:	26th October 2020
Description of Authorised Processing	No personal data is approved to be processed as part of this contract
Subject matter of the processing	
Duration of the processing	
Nature and purposes of the processing	
Type of Personal Data	
Categories of Data Subject	

Annex 2 - Specification

GENERAL INTRODUCTION

The Food Standards Agency (FSA) is a non-ministerial government department governed by a Board appointed to act in the public interest, with the task of protecting consumers in relation to food. It is a UK-wide body with offices in London, Cardiff, Belfast and York.

The FSA is committed to openness, transparency and equality of treatment to all suppliers. As well as these principles, for science projects the final project report will be published on the FSA website (www.food.gov.uk). For science projects we will encourage contractors to publish their work in peer reviewed scientific publications wherever possible. Also, in line with the Government's Transparency Agenda which aims to encourage more open access to data held by government, the FSA is developing a policy on the release of underpinning data from all its science- and evidence-gathering projects. Underpinning data should also be published in an open, accessible, and re-usable format, such that the data can be made available to future researchers and the maximum benefit is derived from it. The FSA has established the key principles for release of underpinning data that will be applied to all new science- and evidence-gathering projects which we would expect contractors to comply with. These can be found at http://www.food.gov.uk/about-us/data-and-policies/underpinning-data.

The objective of the microbiological food safety research themes is to provide robust information on the presence, growth, survival and elimination of pathogenic microorganisms throughout the food chain; the extent, distribution, causes, risks and cost of foodborne disease will also be considered where appropriate.

The main objective from the FSA's Strategic Plan for 2015-2020 is to protect public health from risks which may arise through the consumption of food (including risks caused by the way in which it is produced or supplied) and otherwise to protect the interest of consumers in relation to food. This would include the reduction of foodborne disease to ensure 'food is safe'. This proposed study will assess the impact of heat treatment (different cooking methods) on antimicrobial resistance (AMR) genes that may be present in heat-killed foodborne bacteria and their potential ability to transfer to 'live' bacteria in the human gut and other foods, therefore potentially contributing to AMR in humans. Whilst cooking food thoroughly (at 70°C for 2 minutes or equivalent) will kill vegetative bacterial cells including pathogens and therefore reduce the risk of most forms of food poisoning, there remains uncertainty following ingestion, whether or to what extent AMR gene transfer from 'dead' bacteria to other 'live' bacteria present in the human gut and other food can occur following cooking, including less than thorough cooking such as Sous Vide. This is relevant to the FSA's Science, Evidence and Information Strategy for 2015-2020 as the anticipated outputs will contribute to our understanding of AMR in relation to food and cooking and allow us to ensure that our cooking advice remains appropriate. This in turn will help identify and fill current gaps in knowledge in this area to inform future risk assessments on AMR and identify where further research is required. This is also relevant to the UK National Action Plan on AMR in terms of strengthening the evidence base around food in AMR.

A. THE SPECIFICATION

Background

Antimicrobial resistance (AMR) is a complex issue driven by a variety of interconnected factors enabling micro-organisms to withstand the killing effects of antimicrobial treatments to which they were once susceptible. The overuse or misuse of antibiotics has been linked to increasing the emergence and spread of microorganisms which are resistant to them, rendering treatment ineffective and posing a risk to public health. Unless action is taken now to tackle AMR, it has been estimated that there could be 10 million AMR-related deaths worldwide annually by 2050 and cost up to US $100 trillion in cumulative lost economic output (O'Neill Report, 2014).

Addressing the public health threat posed by AMR is a national strategic priority for the UK and led to the Government publishing both a 20-year vision of AMR and a 5-year (2019 to 2024) AMR National Action Plan (NAP) which sets out actions to slow the development and spread of AMR with a focus on antimicrobials. The NAP used a integrated 'One-Health' approach which spanned people, animals, agriculture and the environment and calls for activities to "identify and assess the sources, pathways, and exposure risks" of AMR. The FSA have and are continuing to contribute to delivery of the NAP through furthering our understanding of the role of the food chain and AMR, conserving the effectiveness of current treatments through the adoption of good hygiene practices and encouraging the food industry to reduce usage of antimicrobials where possible. AMR genes that result in resistance to critically important antimicrobials are of particular concern to the FSA.

Human exposure to drug-resistant bacteria can occur via many routes, including person-to-person transmission, direct contact with animals, and the environment as well as through the food chain (ACMSF, 2018). There has been a longstanding interest in the contribution that the food chain makes to the problem of AMR bacteria in humans. ACMSF (ACMSF, 1999) noted some evidence that AMR foodborne pathogens such as *Salmonella* spp. and *Campylobacter* spp. contribute to human infections but the magnitude of these contributions and the impact of other AMR bacteria, including commensals, remain uncertain.

The FSA currently advises that thorough cooking combined with good hygiene when handling raw meat and food will mitigate the risk to the consumer from AMR bacteria. Whilst thoroughly cooking food will kill AMR bacteria, it will also release DNA into the environment. It is at present unclear whether heat treatment applied to food is sufficient to completely denature any AMR genes that may be present. For example, it has been reported that fragments of bacterial DNA (part of the *eaeA* gene of *E. coli* O157:H7) were not denatured when heated at 95°C for 30 minutes (Wang *et al*., 2014). It has also been shown that naturally competent bacteria are capable of taking up DNA from the environment, which contributes to their evolutionary process (Overballe-Petersen *et al*. 2013). Currently, very little is known about the risks of AMR genes, or other genes such as virulence genes, being transferred from dead bacteria in cooked foods to live bacteria including those present in the human gut. It will also be useful to gain better insight into whether cooking is sufficiently effective in destroying AMR genes (both

plasmid residing and chromosomally residing AMR genes) and therefore subsequent potential uptake by live bacteria.

In addition to the human gut environment, some literature exists to indicate that the food environment could potentially facilitate uptake of DNA by certain bacteria. This could be relevant in the context of this work and is especially worth exploring within the context of AMR genes (Hasegawa *et a*l., 2018).

This proposed review will help increase our understanding of whether and to what extent AMR genes and mobile genetic elements (e.g. plasmids) from 'dead' bacteria in cooked foods can be taken up by 'live' bacteria in the human gut and other foods. This will provide an indication of the potential transfer of AMR genes to humans via food. Current AMR risk assessments do not address the potential for resistantance genes to persist after cooking. This work will provide some key data/information to reduce uncertainty in risk assessment around the persistence (and potential transfer) of AMR genes from 'dead' bacteria in food to 'live' bacteria for example, in other foods, food contact surfaces and the human gut. This in turn will ensure that risk management advice relating to AMR and cooking food is as up-to-date and fully informed as possible, particularly when considering milder heat treatments such as low temperature sous vide, flash frying, slow cooker, rare or light cooking, etc. The focus of this work will be on pathogens, e.g. *Campylobacter*, *Salmonella*, commensal *E. coli, Staphylococcus* and *Enterococcus*.

In 2018, the ACMSF task and finish group recommended as a high priority recommendation that further research and surveillance is needed to continue quantifying the risk of transmission to humans of AMR genes, and particularly those encoding resistance to Critically Important Antimicrobials (CIAs), including plasmid-mediated colistin resistance in organisms from foods of both animal and non-animal origin, both UK-produced and imported. This work will pave the way to beginning to address this important recommendation.

The Specification

Tenders are invited to carry out a critical review of the scientific literature to assess the impact of heat treatment on AMR genes and their potential uptake by other 'live' bacteria.

Overview

We would like to commission a critical review of the scientific literature to enhance our knowledge on the impact of heat treatment on AMR genes and their potential uptake by other bacteria. Particularly, it is important to understand whether cooking food to eliminate bacterial contamination, can also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings including the human gut. This information will improve our understanding in assessing whether cooking food to destroy bacteria also effectively prevents the spread of AMR genes via

food. The work will also help to improve our understanding of the effects of different cooking methods on AMR genes and their transfer from food to humans and to indicate whether the use of milder cooking methods compared to thorough cooking (70°C for 2 mins or equivalent) encourages more effective transfer of AMR genes via food.

Details

Proposals submitted **must** include the following key elements:

Critical review

- A critical review should gather and assess existing data in the literature (including peer-review journals, grey literature, and other sources) to address the following questions/points:

  - Is there evidence to show that heat completely destroys DNA (particularly AMR genes)?

  - Can heat-treated or damaged DNA (AMR genes should be the focus) originating from dead bacteria be taken up by live bacteria? General information relating to whether heat treatment of DNA and particularly AMR genes (including those on mobile genetic elements) affects its ability to be taken up by viable bacteria should be obtained, ideally within a food context. Information relating to transformation frequencies of heat treated/damaged DNA versus intact DNA could be considered.

  - What is the impact of different heat treatments on AMR gene uptake by viable bacteria? Literature should be considered on the effects of bacterial DNA (with a focus on AMR genes) exposure to different heat treatments and subsequent effects on uptake of this DNA by viable bacterial cells. Mobile genetic elements should also be considered. If the literature does not contain such detailed information (e.g. time/temperature combinations), any information obtained should be contextualised in terms of food e.g. cooking conditions where possible. Milder heat treatments such as low temperature sous vide, flash frying, slow cooker, rare or light cooking, etc should also be considered.

  - Is there any evidence of uptake of heat damaged DNA and particularly AMR genes by pathogenic bacteria including *Salmonella, Campylobacter,* commensal *E. coli* and *Staphylococcus* and *Enterococcus.* If this evidence is not directly related to the food/gut environment it should be contextualised where possible. The applicant should focus on the resistance genes relating to CIAs.

- If the literature provides some indication that heat damaged DNA (AMR genes particularly) can be taken up by viable bacteria, then is there any information to suggest that this can also occur in complex environments (e.g. in the presence of large, diverse microbial communities such as the human gut, or complex media such as food (including combined foods) or on food contact materials or biofilms)?

- Is there any evidence to suggest that the behaviour of chromosomal DNA and plasmid DNA in response to heat differs? AMR genes of most concern are likely to be the transferable, plasmid encoded genes.

We anticipate this project starting in September 2020 with the final report being submitted to the FSA in March **2021**.

- The review should collate and consider literature up to December 2020. However, you should be flexible to possibly extend the search end date to ensure that the review is as 'up to date' as possible if the publication of the final report is delayed. The candidates are advised to carry out a quick search of the literature to estimate the number of papers and include this within their proposals. You should also describe how the grey literature will be identified and sourced for the purpose of this review.

- A clear and structured strategy to the critical review process considering the scope, search methods, the search terms, databases to be searched, screening, inclusion-exclusion criteria including key milestone and deliverable dates and methods used to ensure non-biased searching.

- A key component of this work requires expertise in terms of interpreting the findings of the review. However, the findings will also need to be put into context, in terms of whether the findings indicate that there is evidence relating to the risks of AMR genes, or other genes such as virulence genes, being transferred from bacteria in cooked foods to gut bacteria. Therefore, the applicant(s), either individually or collectively in the research group, should have demonstrable expertise in:

  - Designing and carrying out critical reviews of relevant scientific literature.
  - A molecular microbiological background with sound knowledge of AMR, virulence genes, DNA transformation methodology, bacterial competence, PCR based techniques
  - Knowledge relating to bacterial gene transfer mechanisms within complex environments such as the human gut microbiome would be highly desirable
  - Knowledge relating to food technology/processing including cooking methods within the context of food borne pathogens and AMR would be highly desirable

- Given the current situation with COVID-19, the applicants should consider the possible risk to the delivery of the study and pose actions to mitigate the foreseen risks as part of the risk register within their proposal.

Given that this list of expertise is quite extensive, the FSA strongly encourages a collaborative proposal to ensure all the relevant background and expertise is suitably covered by the researchers to undertake this proposed work.

Outcomes

It is anticipated that the following will be delivered to the FSA as part of this work:

- A full technical report addressing the relevant areas of the study which is suitable for publication on the FSA website. The report should include a lay summary, an executive summary, introduction (including the background and aims/objectives of the review), methodology, findings, discussions, conclusions, list of evidence gaps, recommendations for further work, references and an appendices section. The final report will need to be structured and formatted in accordance to guidelines from the FSA. Please note that the final report should be submitted to the FSA **by March 2021** and will undergo a peer-review process before it can be accepted by the FSA. A draft report should be submitted at least 6 weeks before the final report is due to allow FSA officials sufficient time to comment.

- The critical review should be both transparent and reproducible. A full database of all the relevant publications included in the critical review should be provided to the FSA. The database should be in a format suitable for publication on the FSA website e.g. in an accessible format (for example CSV or Excel).

- Publication of findings from this study in the peer reviewed literature and presentations at scientific conferences are encouraged by the FSA. Such material will need to be approved by the FSA prior to being submitted to the journal. It is important that the researcher(s) notify the FSA of the publication date for any papers arising from this study at the earliest opportunity especially if the findings are contentious and therefore likely to generate media interest.

- The findings of this work are likely to be presented at a future FSA AMR ‘show and tell’ event, ACMSF (or AMR sub-group) meetings and at a stakeholder meeting if needed.

- Contractors will be expected to assist the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on news story.

Collaborative applications with an appropriate management framework are encouraged to promote well-balanced, innovative proposals that offer value for money and make use of the best available research and analytical approaches.

References

O'Neill, (2014), Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations

https://amr-review.org/

ACMSF Task & Finish Group Report on AMR, 2018 - Antimicrobial resistance in the food chain; research questions and potential approaches
https://acmsf.food.gov.uk/sites/default/files/acm_1278_amr_report.pdf

The UK's 20 Year Vision for antimicrobial resistance, 2019
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/773065/uk-20-year-vision-for-antimicrobial-resistance.pdf

Tackling antimicrobial resistance 2019–2024 -The UK's five-year national action plan
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf

Wang, X., Lim, H.J., Son, A. (2014) Characterization of denaturation and renaturation of DNA for DNA hybridization. Environ Health Toxicol., Sep 11;29: e2014007.

https://www.ncbi.nlm.nih.gov/pubmed/25234413

Overballe-Petersen, S., Harms, K., Ludovic, A. A., Orlando , J., Moreno Mayar, V., Rasmussen, S., Dahld, T.W., Rosing, M.T., Poole, A.M., Sicheritz-Ponten, T., Brunak, S., Inselmann, S., de Vriesg, J., Wackernagel, W., Pybush, O.G., Nielsen, R., Johnsen, P.J. Nielsen, K.M. and Willerslev, E. (2013) Bacterial natural transformation by highly fragmented and damaged DNA. PNAS 110 (49):19860-19865.

https://www.pnas.org/content/pnas/110/49/19860.full.pdf

Hasegawa, H., Suzuki, E., Maeda, S. (2018) Horizontal Plasmid Transfer by Transformation in *Escherichia coli*: Environmental Factors and Possible Mechanisms. Front Microbiol. 2018 (9): 2365.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6180151/

Openness:

FSA has values and specific policy on being open and transparent, which includes publishing the full dataset of its research and surveillance studies. Both the lead contractor and their sub-contractors must agree to this openness policy. Any potential issues with this should be highlighted within the proposals.

General Data Protection Regulation (GDPR):

Tenderers should also note that the EU's General Data Protection Regulation (GDPR) was introduced in the UK from the 25th of May 2018. Tenderers are therefore asked to consider what additional measures may need to be taken in order to comply with the new regulatory regime for data protection and to include in their proposals an explanation of how they intend to implement these measures.

In particular, the processor (the lead contractor) must:

- process the personal data only on the documented instructions of the Controller (the FSA);
- comply with security obligations equivalent to those imposed on the Controller (implementing a level of security for the personal data appropriate to the risk);
- ensure that persons authorised to process the personal data have committed themselves to confidentiality or are under an appropriate statutory obligation of confidentiality;
- only appoint Sub-processors (any sub-contractors) with the Controller's prior specific or general written authorisation, and impose the same minimum terms imposed on it on the Sub-processor; and the original Processor will remain liable to the Controller for the Sub-processor's compliance. The Sub-processor must provide sufficient guarantees to implement appropriate technical and organisational measures to demonstrate compliance. In the case of general written authorisation, Processors must inform Controllers of intended changes in their Sub-processor arrangements;
- make available to the Controller all information necessary to demonstrate compliance with the obligations laid down in Article 28 GDPR and allow for and contribute to audits, including inspections, conducted by the Controller or another auditor mandated by the Controller - and the Processor shall immediately inform the controller if, in its opinion, an instruction infringes GDPR or other EU or member state data protection provisions;
- assist the Controller in carrying out its obligations with regard to requests by data subjects to exercise their rights under chapter III of the GDPR, noting different rights may apply depending on the specific legal basis for the processing activity (and should be clarified by the Controller up-front);
- assist the Controller in ensuring compliance with the obligations to implementing a level of security for the personal data appropriate to the risk, taking into account the nature of processing and the information available to the Processor;

- assist the Controller in ensuring compliance with the obligations to carry out Data Protection Impact Assessments, taking into account the nature of processing and the information available to the Processor; and

- notify the Controller without undue delay after becoming aware of a personal data breach.

At this moment in time, the FSA does not envisage the need to collect any personal data as part of this study.

Annex 3 – Supplier's Technical Proposal

Tender Application form for a project with the Food Standards Agency

- Applicants should complete each part of this application as fully and as clearly as possible
- Brief instructions are given in the grey boxes at the start of each section.
- Please submit the application through the Agency's eSourcing Portal (Bravo) by the deadline set in the invitation to tender document.

LEAD APPLICANT'S DETAILS

[redacted]

TENDER SUMMARY

TENDER TITLE

Assessing the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria

TENDER REFERENCE	**FS301059**		
PROPOSED START DATE	01/11/2020	**PROPOSED**	30/05/2021

1: TENDER SUMMARY AND OBJECTIVES

A. TENDER SUMMARY

Please give a brief summary of the proposed work in no more than 400 words.

The overall aim of this project is to carry out a critical review of the scientific literature to assess the impact of heat treatment on AMR genes and their potential uptake by other 'live' bacteria. It will focus particularly (but not exclusively) on what scientific evidence exists that provides an understanding on whether cooking (heating) food to eliminate bacterial contamination can also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings including the human gut. This information will improve the Agency's understanding in assessing whether heat treatment of food to destroy bacteria also effectively prevents the spread of AMR genes via food. The

work will also help to improve the Agency's understanding of the effects of different cooking (heat treatment) methods on AMR genes and their transfer from food to humans and to indicate whether the use of milder cooking (heat treatment) methods compared to thorough cooking (70°C for 2 mins or equivalent) encourages more effective transfer of AMR genes via food.

It is proposed that the review question will be: "Do heat treatments applied to eliminate bacterial contamination in foods also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings, including the human gut and other foods?"

The project technical report will critically review the available scientific literature to assess the impact of heat treatment on AMR genes and their potential uptake by other 'live' bacteria, and identify, highlight, and recommend where future surveillance activities are needed to plug important evidence gaps. A database of the publications included in the review will also be provided. The proposed review will take 6 months to complete.

The project team (consisting of food process engineers from the Grimsby Institute and microbiological and food safety experts from the University of Lincoln) have experience of carrying out such critical reviews and risk assessments, and expertise in food processing technologies and AMR.

B. OBJECTIVES AND RELEVANCE OF THE PROPOSED WORK TO THE FSA TENDER

OBJECTIVES

Please detail how your proposed work can assist the agency in meeting it stated objectives and policy needs. Please number the objectives and add a short description. Please add more lines as necessary.

OBJECTIVE NUMBER	OBJECTIVE DESCRIPTION
01	**LITERATURE SEARCH:** To carry out a structured literature search of appropriate bibliographic databases and sources in order to compile a broad data set of as many potentially relevant articles pertaining to the impact of heat treatment on antimicrobial resistance genes (ARG) that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods as possible. A record of all identified articles will be complied and recorded.
02	**ARTICLE SCREENING:** To screen the compiled data set of potentially relevant articles in order to select relevant articles for data extraction. To ensure transparency a record will be kept of all articles determined as not relevant and reasons for their exclusion.
03	**DATA EXTRACTION AND ANALYSIS:** To extract, and analyse, pertinent data from articles that have been selected as containing important information on the impact of heat treatment on antimicrobial resistance genes (ARG) that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods**.**
04	**DATA SYNTHESIS AND REVIEW COMPLETION:** To synthesise the extracted data from articles into a formal review report in order to establish what existing data and understanding there is on the impact of heat treatment on antimicrobial resistance genes (ARG) that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods. The review will identify what is known and what data gaps remain and provide recommendations for further work.
05	**DISSEMINATION:** To disseminate the findings of the project to key stakeholders to inform them of what realistic actions are required to reduce the risks associated with AMR in heat treated (and cooked) foods and where further work is required.

2: DESCRIPTION OF APPROACH/SCOPE OF WORK

A. APPROACH/SCOPE OF WORK

Please describe how you will meet our specification and summarise how you will deliver your solution. You must explain the approach for the proposed work. Describe and justify the approach, methodology and study design, where applicable, that will be used to address the specific requirements and realise the objectives outlined above. Where relevant (e.g. for an analytical survey), please also provide details of the sampling plan.

Project aim and scope

The overall aim of this project is to carry out a broad critical review of the available scientific literature to assess the impact of heat treatment on antimicrobial resistance genes (ARG) that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods.

Background and rationale

For the interpretation of AMR in this study, the WHO definition will be applied (WHO, 2018): "Antimicrobial resistance is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it. Resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g. antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others".

Antimicrobial resistance (AMR) and AMR genes are a major public health issue worldwide. Resistance is a complex 'one health' issue driven by a variety of interconnected factors enabling microorganisms to withstand antimicrobial treatments to which they were once susceptible (FSA, 2018). It is recognised that anthropogenic, commensal, and environmental microorganisms all contribute to the reservoir of ARGs collectively forming the antibiotic resistome (Wright, 2007).

In order for a bacteria to develop resistance to any antimicrobial agent, the bacteria must have AMR genes. Bacteria may be resistant to just one antimicrobial or to many, with cross resistance depending on which AMR genes and other mechanisms of resistance are present (permeability barriers and efflux pumps etc). This can make infections caused by these organisms difficult to treat and cause infections to persist with recognised extra costs (Likotrafiti et al., 2018). Food can be contaminated with AMR bacteria and/or AMR genes in several ways (Verraes et al., 2013): (1) through the presence of AMR bacteria on food treated by anti-microbials during agricultural production; (2) the possible presence of AMR genes in bacteria that are intentionally added during the processing of food (starter cultures, probiotics, bio-conserving microorganisms and bacteriophages); (3) through cross-contamination with AMR bacteria and genes during food processing. Much attention has been paid to the potential transmission of AMR among food and human through horizontal antimicrobial gene transfer. In addition, the cross-stress adaptation phenomenon of AMR bacteria to heat have been reported, which lead to potential risk since these resistant bacteria can persistently colonize and recurrently contaminate food (Oniciuc et al., 2019). An important difference between the transmission of non-resistant pathogens and AMR bacteria is that resistance genes may be disseminated by non-pathogenic bacteria, which may then subsequently transfer those resistance genes to human pathogens after the food is consumed (Bengtsson-Palme, 2017).

Regarding the published literature on the impact of heat treating food on AMR bacteria/genes, without prejudicing the findings of the proposed review, a preliminary scan of published data immediately highlights a number of issues that clearly need to be addressed in the full review.

It is fully accepted that heat treatments such as sterilization, UHT treatment, and (full) pasteurization under well-defined time/temperature combinations will eradicate /kill vegetative bacterial cells, including those of AMR bacteria. Industrial, food service, domestic or institutional cooking is normally sufficient to eliminate the effect of pathogens from food but it remains unclear whether thorough cooking destroys all components of AMR bacteria or AMR genes. Complete AMR gene DNA or even fragments of bacterial DNA that survive from chromosomal or plasmid DNA may be capable of transfer to other microbiota in the human gut and be incorporated to become a functional source of a novel bacterial genome. There is some literature (Aubry-Damon et al., 2004; Hart et al., 2006; Ramchandani et al., 2005) that lends weight to this hypothesis.

Dead cells cannot pass AMR genes to other bacteria by conjugation or transduction (Verraes et al., 2013) but as soon as DNA fragments have been released, AMR genes may, theoretically, be transferred by transformation (McMahon et al., 2007; Verraes et al., 2013; Le Devendec et al., 2018; Pérez-Rodríguez & Taban, 2019). However, the process of transformation occurs with low frequency

and is subject to a large number of requirements mostly observed in very controlled laboratory conditions.

Interestingly, a number of studies have also demonstrated that AMR gene fragments can persist after heat treatments, including pasteurisation treatments. For example, Wang et al. (2014) reported that fragments of bacterial DNA (part of the eaeA gene of *Escherichia coli* O157:H7) were not denatured when heated at 95°C for 30 minutes. While Taher et al. (2020) recently reported that a standard milk pasteurisation treatment (63.5°C for 30 min) was not sufficient in inactivate AMR genes (blaZ, mecC and tetK) of staphylococci and, in addition, would induce a viable but non-culturable (VBNC) state of these bacteria. It has also been shown that naturally competent bacteria are capable of taking up DNA from the environment, which contributes to their evolutionary process (Overballe-Petersen et al. 2013). Though, while Le Devendec et al. (2018) could not completely exclude the possibility of AMR genes being transferred from heat-inactivated *E. coli* via natural transformation during food preparation, they considered that given the "infrequency of natural transformation and low probability of a whole resistance gene reaching the lower intestinal tract", they believed it unlikely for indigenous *Enterobacteriaceae* from the digestive microbiota to be transformed by DNA from heat-inactivated foodborne bacteria. It is clear that the capacity for acquisition of AMR genes by gut microbiota deserves more intensive study (Buffie & Pamer, 2013; Taher et al., 2020). In addition to the human gut environment, some literature exists to indicate that the food environment could potentially facilitate uptake of DNA by certain bacteria. This could be relevant in the context of this work and is especially worth exploring within the context of AMR genes (Hasegawa et al., 2018).

Studies by Walsh et al. (2001), Bertolatti et al. (2001), Stopforth et al. (2008), Lianou & Koutsoumanis (2013) Akhtar et al. (2016) and Komora et al. (2017), amongst others have indicated that AMR bacteria, such as *E. coli*, *Listeria monocytogenes*, *Salmonella*, *Staphylococcus aureus*, do not exhibit enhanced thermal resistance characteristics. Although studies by Walsh et al. (2005) on strains of *Salmonella enterica* serovar typhimurium DT104 have indicated that some strains of AMR bacteria may have enhanced thermal characteristics. Conversely Duffy et al. (2006) reported a more heat sensitive naturally Multi-Antibiotic Resistant (MAR) isolate of *E. coli* O157:H7. This indicates, as may be expected, that there are differences in thermal tolerance between different bacteria, serotype or strain, and different substrates and that when formally reviewing such data these details must be looked at carefully. However these studies essentially did not address AMR genes.

Studies suggest that increased use of sublethal, rather than lethal food preservation systems may be more important than was previously considered for the development and dissemination of AMR (Verraes et al., 2013; Capita & Alonso-Calleja, 2013; Ferri et al., 2017). Under minimal processing or preservation treatment conditions, sub-lethally damaged or stressed cells can be maintained in the food, inducing AMR build-up and enhancing the risk of resistance transfer (Verraes et al., 2013). Stress conditions such as heat stress among others may trigger several mechanisms in bacterial cells, e.g., stress adaptation, cellular repair, application of response mechanisms and enhanced virulence (Wesche et al., 2009). McMahon et al. (2007), for example, showed that sublethal high temperature induced heat stress reduced antimicrobial resistance in food-related pathogens such as *E. coli*, *S.* typhimurium, and *S. aureus*, while increased salt or reduced pH conditions on the other hand increased the phenotypical antimicrobial resistance. AMR genes that are present in partly inactivated, stressed cells may be transferred to commensals and pathogens, both in the foodstuff and after ingestion in the digestive system of humans (Verraes et al., 2013). This may be achieved either by conjugation, when resistance is located on mobilizable elements, or by transformation and transduction, however to a lower degree. It has been observed in laboratory trials that processing stresses (e.g., high or low temperatures, osmotic and pH stress) can increase horizontal transfer of antibiotic resistance genes by conjugation (McMahon et al., 2007) or transformation (Rodrigo et al., 2010) mechanisms. This is an important issue that will be addressed by this review. There is clearly a concern that sub-lethal food processing designed treatments might play a role in an increase in AMR since not all heat treatments are lethal. There is clearly a need to define lethal parameters and identify "sub-lethal heat treatments" that have been adopted by the industry. To do this heat treatments need to be fully characterised, i.e. what endpoint temperatures and times would be expected in foods subject to different heat treatment.

Bacterial outer membrane vesicles (OMVs) are proteo-liposomal nanoparticles produced by both Gram-negative and Gram-positive bacteria generally in response to environmental stresses. They originate from the outer leaflet surface of the bacteria and their composition and content reflects the bacteria's membrane and cytoplasm. Although, there is ample evidence that packaging of proteins, metabolites, and toxins into membrane vesicles does occur, some reports also show chromosomal

DNA (Bitto et al., 2017) or plasmid DNA (Rumbo et al., 2011) is incorporated into membrane vesicles and may be part of a mechanism for long-distance movement to other 'live' bacteria or even eukaryotic cells. The membrane vesicles protect the 'cargo' from degradation by other bacteria, the host organism, or environmental factors. Vesicles appear to be enabled to serve specialized functions tailored to changes in heat treatment or other challenging environments and have roles in quorum sensing, biofilm formation and nutrient acquisition. The function of membrane vesicles in transfer of DNA among bacteria is an emerging area of interest and the project will assess what existing evidence there is that AMR genes can survive heat treatment through this strategy.

The is evidence that the role of biofilms should be considered in the project review, since there is literature about the protective effects of extracellular polymeric saccharides (EPS) on antimicrobial action of various bacteria. Thus AMR genes within AMR bacteria deep within a protective EPS might be unaffected by mild heat treatments and survive intact to transfer to viable cells compared with unprotected bacteria within the gut microbiota. Specifically a paper by Hu et al. (2019) describes the lateral transfer of AMR genes from biofilms into competent bacteria, using AMR genes carried by plasmids (pUC19, pHSG298, and pHSG396) into competent *E. coli* cells with and without EPS. Transformant numbers and transformation efficiency for *E. coli* without EPS were up to 29 times of those with EPS at pH 7.0 in an aqueous system. The EPS removal further increased cell permeability in addition to the enhanced cell permeability by Ca2+, which could be responsible for the enhanced lateral transfer of the AMR genes. Experiments showed that EPS could strongly bind to plasmid DNA in the presence of Ca2+ and therefore concluding that the binding of plasmids with EPS hindered the lateral transfer of plasmid-borne AMR genes.

How this proposal meets the FSA specification

The proposed study has been structured in line with the FSA specification and is squarely aimed at addressing all of the key elements requested in the FSA specification documents, namely the review will:

- Aim to identify and critically review what scientific evidence is available that heat treatments of food which eliminate bacterial contamination can also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings including the human gut.
- Gather and assess existing data in the literature (including peer-review journals, grey literature, and other sources) up to December 2020 (but will be flexible to extend that search end date should the publication of the final report be delayed).
- Include not only clinically important ESKAPE and other pathogenic organisms with AMR/industrial relevance (such as *Acinetobacter baumannii*, *Campylobacter*, *Enterobacter*, *Enterococcus faecium*, *Klebsiella pneumoniae*, *Listeria*, *Salmonella*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*), but also non-pathogenic AMR flora (such as *Enterococcus faecalis,* commensal *Escherichia coli*).
- Address the following key questions cited in the FSA specification:
    - Is there compelling evidence to show that heat completely destroys DNA (particularly AMR genes either as naked DNA or within AMR bacteria)? What evidence is there of thermal degradation in various DNA contexts?
    - Can heat-treated or damaged DNA (AMR genes will be the focus) originating from dead bacteria be taken up by live bacteria? General information relating to whether heat treatment of DNA and particularly AMR genes (including those on mobile genetic elements - plasmids/transposons integrons etc) affects its ability to be taken up by viable bacteria will be obtained, ideally within a food context. Information relating to transformation frequencies of heat treated/damaged DNA versus intact DNA will also be considered.
    - What is the impact of different heat treatments on AMR gene uptake by viable bacteria? Literature will be considered on the effects of bacterial DNA (with a focus on AMR genes) exposure to different heat treatments and subsequent effects on uptake of this DNA by viable bacterial cells. Mobile genetic elements will also be considered. If the literature does not contain such detailed information (e.g. time/temperature combinations), any information obtained will be contextualised in terms of food, e.g. cooking conditions, where possible. Milder heat treatments such as low temperature sous vide, flash frying, slow cooker, rare or light cooking, etc will also be considered.

    - Is there any evidence of uptake of heat damaged DNA, and particularly AMR genes, by pathogenic and non-pathogenic bacteria? If this evidence is not directly related to the food/gut environment it will be contextualised where possible. The review will focus on the resistance genes relating to the Critically Important Antimicrobials (CIAs).
    - If the literature provides some indication that heat damaged DNA (AMR genes particularly) can be taken up by viable naturally competent bacteria in the laboratory, then is there any information to suggest that this can also occur in complex environments (e.g. in the presence of large, diverse microbial communities such as the human gut, or complex media such as food (including combined foods) or on food contact materials or biofilms)?
    - Is there any evidence to suggest that the behaviour of chromosomal DNA and plasmid DNA in response to heat differs? AMR genes of most concern are likely to be the transferable, plasmid encoded genes.
- In addition to the key questions cited in the FSA specification, we believe it should also consider:
    - Is there any evidence on the role of proteins in the transfer of AMR genes from AMR bacteria subjected to heat treatments? Proteins are more vulnerable to heat than DNA but have multiple functions and most of the transfer functions will not occur if they have degraded, such as due to heat damage.
    - Is there any evidence on the role of outer membrane vesicles (OMVs) in the survival and transfer of AMR genes from AMR bacteria subjected to heat treatments? OMVs are extracellular sacs containing biologically active products, such as DNA, proteins, cell wall components, and toxins. There is some evidence that they could be an important route of survival of plasmids and/or Chromosomal DNA.
- Provide some key data/information to reduce uncertainty in risk assessment around the persistence (and potential transfer) of AMR genes from 'dead' bacteria in food to 'live' bacteria for example, in other foods, food contact surfaces and the human gut. This in turn will ensure that risk management advice relating to AMR and heat treating (cooking) food is as up-to-date and fully informed as possible, particularly when considering milder heat treatments such as low temperature sous vide, flash frying, slow cooker, rare or light cooking, etc.

The review will focus on critically important AMR genes, using the WHO list of critically important antimicrobials for human medicine (WHO, 2019) are a reference. We will focus firstly on the highest priority classes of antimicrobials on the list and decide within those classes which antimicrobials and hence resistance genes to narrow down and focus on and provide a rational for the decisions. The approach will then consider the high priority classes of antimicrobials on this list and their resistance genes.

To ensure that the review is both transparent and reproducible a list all the databases and key search terms used will be documented and any indicative criteria for inclusion and rejection based on the quality of the studies being considered. Finalised key search terms will be agreed with the Agency prior to project initiation. A full database of all the relevant articles will be provided to the Agency. The database will be in a format suitable for publication on the FSA website, e.g. in an accessible format (for example CSV or Excel).

The proposed study has been structured in line with the specification and is squarely aimed at addressing all of these key elements. If other elements not listed are identified as being significant regarding the impact of heat treatments on AMR bacteria/genes during the review these will be discussed with the Agency and incorporated into the work programme if considered appropriate.

The project team will work closely with Agency representatives throughout the progress of the project to ensure the maximum visibility and usability of all findings and dissemination materials produced by the project.

Proposed scientific approach

The proposed work will carry out a broad critical review of the available scientific literature to assess the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria.

The project will be carried out by a project team of experienced food process scientists and engineers from the Food Refrigeration & Process Engineering Research Centre (FRPERC) at the Grimsby

Institute of Further and Higher Education (GIFHE) and experts on food microbiology and antimicrobial resistance from the University of Lincoln. Additional AMR expertise in a molecular context will be provided by Professor Nicola Williams from the University of Liverpool who will act as an external AMR consultant/expert advisor to the project, particularly on aspects AMR aspects in a molecular context. Her expertise will be sought over the course of the project as and when such specific expertise is required. The project team has extensive experience and expertise in the food chains from farm-to-fork, having, in their time, carried out studies on the control of microbial hazards using heat on foods at all stages from the factory to the home. They are thus ideally placed to ensure that the findings of this review are robust and relevant to practices used by the UK from processing to the home and to the needs of the key stakeholders.

The staff who will be working on this project all have experience and a long track record of designing and carrying out similar critical literature reviews (including for the Agency) and practical experience and expertise relating to food technology/processing including cooking methods within the context of food borne pathogens. Examples of reviews (or projects including reviews of literature) that they have led or been involved, since 2000, include:

- James, C., Purnell, G., & James, S. J. (2003). Review of the use of ozone in red meat and poultry processing. Food Standards Agency (FSA) project no. ZM0104.
- James, C., James, S. J., & Buncic, S. (2004). Review of potential effects of transporting meat above 7°C. Food Standards Agency (FSA) project no. ZM01011.
- James, C., Pinho, R. M., & James, S. J. (2006). Safety implications of the manufacture of minced meat from aged meat. Food Standards Agency (FSA).
- James, C., Vincent, C., de Andrade Lima, T. I., & James, S. J. (2006). The primary chilling of poultry carcasses – a review. *International Journal of Refrigeration*, 29:6, 847-862.
- Newell, D. G., Allen, V., Elvers, K., Dorfper, D., Hanssen, I, Jones, P., James, S., Gittins, J., Stern, N., Davies, R., Connerton, I., Pearson, D., & Salvat, G. (2008). B15025: A critical review of interventions and strategies (both biosecurity and non-biosecurity) to reduce Campylobacter on the poultry farm. Food Standards Agency (FSA) project no. B15025.
- James, C., Purnell, G., & James, S. J. (2013). Description of the processes used in the UK to manufacture MSM and former DSM meat products from poultry and pork and an initial assessment of microbiological risk. Food Standards Agency (FSA) project no. FS503001.
- James, C., Derrick, S., Purnell, G., & James, S. J. (2013). Review of the risk management practices employed throughout the fish processing chain in relation to controlling histamine formation in at-risk fish species. Food Standards Agency (FSA) project no. FS241055.
- James, C., Daramola, B., Dudkiewicz, A., Reyers, F., Purnell, G., Turner, R., James, S. J., & Braybrooks, V. (2014). Qualitative Risk Assessment to support a policy decision on partially-eviscerated (effilé) poultry production. Food Standards Agency (FSA) project no. FS101044.
- James, C., Purnell, G., & James, S. J. (2015). A review of novel and innovative freezing technologies. *Food and Bioprocess Technology*, 8, 1616-1634.
- James, C., Onarinde, B. A., & James, S. J. (2017). The use and performance of household refrigerators: A review. *Comprehensive Reviews in Food Science and Food Safety*, 16(1), 160–179.
- James, C., Daramola, B., Chu, J., Dudkiewicz, A., Purnell, G., & James, S. J. (2018). Exploring the potential for technology to support agency objectives in meat operations. Food Standards Agency (FSA) project no. SEP-EOI-02.

A mixed-method knowledge synthesis approach will be adopted for this critical review, based on the approaches used by Newell et al., (2008), Thomas et al. (2012), Mateus et al. (2016), and FAO/WHO (2016). This should enable a critical review to be completed that is as unbiased, and as evidence-based as possible. The use of a structured and transparent approach to identify, assess, and synthesize available evidence on the impact of heat treatment on AMR genes and their potential uptake by other 'live' bacteria should provide more credible and reliable evidence to the Agency than a traditional narrative review. Although it is anticipated that the review will incorporate some traditional narrative aspects where appropriate (e.g. when highlighting data gaps, and identifying, highlighting, and recommending areas for further work). The approach will follow that detailed in the Agency's specification, i.e.:

- The review will adopt a comprehensive search strategy considering all available evidence in the public domain, including peer-reviewed articles, grey literature (e.g. government and industry reports), relevant government reports (e.g. FSA published studies, ACMSF reports,

etc.), European and International literature (e.g. the EFSA Scientific Opinions, WHO reports) up to December 2020. This will include previously published systematic and critical reviews, and risk assessments, as well as primary research.

- The proposal lists the databases and key search terms to be used and also any indicative criteria for inclusion and rejection based on the quality of the studies being considered. Finalised terms will be agreed with the Agency prior to project initiation.
- The review will focus on identifying and reviewing both quantitative and qualitative information on the impact of heat treatment on AMR genes that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods. The criteria for selection and non-selection of relevant information for consideration in the review will be included in the final report.

The project has five objectives:

- Objective 1: Literature search: To carry out a structured literature search of appropriate bibliographic databases and sources in order to compile a broad data set of as many potentially relevant articles.
- Objective 2: Article screening: To screen the compiled data set of potentially relevant articles in order to select important articles for data extraction.
- Objective 3: Data extraction and analysis: To extract, and analyse, pertinent data from the articles that have been selected as clearly relevant.
- Objective 4: Data synthesis and review completion: To synthesise the extracted data from articles into a formal review report in order to establish what existing data and understanding there is on the impact of heat treatment on AMR genes that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods.
- Objective 5: Dissemination: To disseminate the findings of the project to key stakeholders to inform them of what realistic actions are required to reduce the risks associated with AMR in heat treated (and cooked) foods and where further work is required.

To realise **Objective 1**, the **literature search**, the project will follow the following key approaches.

It is proposed that the review question will be:

"Do heat treatments applied to eliminate bacterial contamination in foods also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings, including the human gut and other foods?"

The key elements of the question (PIO): Population (P), Intervention (I), and Outcome (O) are:

- The **population** of interest include pathogenic and non-pathogenic AMR bacteria (such as *Acinetobacter baumannii*, *Campylobacter*, *Enterobacter*, *Enterococcus faecium* and *faecalis*, commensal *Escherichia coli*, *Klebsiella pneumoniae*, *Listeria*, *Salmonella*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*)* and specifically their AMR genes.
- Any heat treatment **interventions** applied to foods are considered relevant, such as pasteurisation, sterilisation, cooking treatments (e.g. hot air (oven), steam, hot water (boiling, blanching), hot fat or oil (shallow or deep frying), grilling, radiant, dielectric (microwave), extrusion, pressure, retort, etc.), and mild heat treatments (e.g. low temperature sous vide, flash frying, slow cooker, rare or light cooking, hot smoking, etc.)
- Relevant **outcome measures** for interventions are does the intervention induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other locations including the human gut and other foods.

* The search will not be restricted to this list alone, a full list of organisms will be agreed with the FSA Project Officer prior to commencing the literature search. Also if other microorganisms are identified during the course of the project we will consider adding these, following consultation with the FSA Project Officer.

All AMR genes of immediate or emerging concern will be considered. A search for specific AMR genes will not be carried out in the initial literature search, since there are so many of potential concern, some with rapid mechanisms for transfer. We intend to build a list of immediate and potential AMR genes of concern as the literature search and analysis progresses. The review will focus on critically important

AMR genes, using the WHO list of critically important antimicrobials for human medicine (WHO, 2019) as a reference. We will focus firstly on the highest priority classes of antimicrobials on the list and decide within those classes which antimicrobials and hence resistance genes to narrow down to and focus on and provide a rational for the decisions. The approach will then consider the high priority classes of antimicrobials on this list and their resistance genes.

Initial Consultation

Before commencing the literature search, the review question, keywords, scope of search, and eligibility criteria will be agreed with the Agency. Suggested keywords, scope of search, and eligibility criteria are listed below.

Inclusion/Exclusion Criteria

All evidence on the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria available in the public domain will be considered, including primary research, previously published reviews, and risk assessments. The literature search will be restricted to English-language peer-reviewed journals, books, reports, or articles. Grey literature (e.g. government and industry reports) will also be considered. The results will be refined by relevance to keywords. Post-2000 articles will be given precedence, but older articles may be considered for background information.

Search Engines/Databases

The following databases / search engines will be used:

- Web of Science from 1990-current
- MEDLINE from 1990-current
- Scopus from 1990-current
- PubMed.Net from 1990–current
- Google Scholar from 1990-current
- EMBASE from 1990-current
- CAB abstracts from 1990-current
- ScienceDirect from 1990-current
- Biomed Central from 1990-current
- Food Science and Technology abstracts from 1990-current

If any other relevant databases are identified in the early stages of the project, these will be considered and include if agreed of importance by the project team and FSA Project Officer. The bibliographic databases to be used include food safety and processing, public health and agriculture subject areas. In addition, search verification will be conducted by reviewing a reference list of a selection of relevant original research, review articles and book chapters.

Supplementary Collation Methods

In addition to the database searches, collation will be supplemented by:

- Searching through relevant government reports, e.g. FSA published studies, ACMSF reports, etc.
- European and International literature, e.g. EFSA scientific opinions, WHO reports, etc.
- Searching of key journals, e.g. International Journal of Food Microbiology, Journal of Food Protection, etc.
- Searching articles, e.g. Environmental Health News Magazine/Online.
- Contacting experts.
- Reference list tracking, Reference lists of all studies selected for inclusion will be searched to identify further relevant studies.
- A public "call for data".

Boolean Operators

All search terms will be chosen according to the population (key pathogens), heat treatment (search terms broadly listed below) and will be combined using Boolean operators. 'AND' will be applied where it is necessary for both terms to be used. 'OR' will be applied when either/or could be used. Searches will be limited using the 'NOT' Boolean operator. The search algorithm will be pre-tested in Web of Science to ensure that a known list of relevant articles could be sufficiently identified.

Keywords and search string

Finalised keywords will be agreed with the Agency prior to project initiation. A suggested search string is:

("antimicrobial resistan*" OR "antibiotic resistan*" OR "antibacterial resistan*" OR multirestan* OR "multidrug resistan*" OR "multi-drug resistan*" OR "multiantibiotic resistan*" OR AMR OR MDR OR MAR OR AR OR AMRG) AND (Acinetobacter OR Campylobacter OR commensal OR Enterobacter OR Enterococcus OR "Escherichia coli" OR "E. coli" OR Klebsiella OR Listeria OR Salmonella OR Staphylococcus OR pathogen* OR Pseudomonas) AND (heat OR thermal OR pasteuri* OR sterili* OR UHT OR HTST OR "hot water" OR steam OR boil* OR blanch* OR oven OR roast* OR fry OR "hot fat" OR grill* OR broil* OR microwave* OR "pressure cook*" OR retort OR "sous vide" OR cook* OR inactive* OR consumption OR sublethal OR "human gut" OR intestin* OR "bacterial outer membrane vesicle*" OR OMV or biofilm* OR "extracellular polymeric saccharide*" OR EPS)

in Article title

OR

in Abstract

OR

in Subject headings

Any searches of the literature and criteria used will be documented at all times to allow replication of the methodology used.

Collation of articles

For all searches, citations and abstracts will be uploaded from each of the electronic databases into Covidence [https://www.covidence.org] (this SR tool has been chosen because a number of reviews of SR tools (Kellermeyer et al., 2018; Van der Mierden et al., 2019; Harrison et al., 2020) have highlighted it as the most comprehensive SR tool package and one of the most easy to use). The references will be processed using the 'find duplicates' automated functionality of the program and the duplicates will be removed.

To ensure that all of the pertinent papers are identified, the search strategy will be verified by checking the generated list of references against the cited reference lists of a random selection of five articles for all searches. To ensure completely random selection of articles, the papers will be sorted by author name and each assigned a sequential number. The formula =n * rand() will be used in Excel (version 16; Microsoft Corp. Redmond, WA, USA) to generate a list of random numbers corresponding to the papers. The 'cited by' functionality of the Web of Science will then be used to identify that articles published after the five randomly-selected references, which cited these papers, have been included in the search-generated reference list.

Objective 1 will produce a database consisting of collated citations and abstracts of all articles identified in the literature search.

To realise **Objective 2**, **article screening**, the project will follow the following key approaches.

Selection of articles for data extraction

The relevance of each unique citation will be assessed at the title and abstract level using an a priori developed form. The form will include one key question to determine the citation's relevance to the review question and eligibility criteria. Abstracts will be excluded if:

- They contain no relevant data on the impact of heat treatment on antimicrobial resistance genes that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods.
- Are in a language other than English.
- Duplicate data.
- Measure irrelevant interventions (no heat treatment), outcomes, or populations or samples.

The criteria will be independently applied to the abstract of each paper by at least two members of the five member project team. For each citation, a consensus will be reached that the article is relevant for

inclusion. Arbitration by a third member of the project team will be used to settle conflicting appraisals. Full articles will be obtained for all abstracts that pass the inclusion criteria. To ensure transparency a record will be kept of all articles determined as not relevant.

A preliminary search of articles on heat treatment and AMR genes (using the suggested keyword search) has shown that the initial broad literature search will identify a large number (10,091 – Web of Science) of complex and diverse articles that may be relevant. However, having looked through a sub-section of the abstracts that this preliminary broad search identified it is expected that articles specifically related to the impact of heat treatments on AMR genes will possibly only number in the low hundreds. In order to prevent data saturation without analysing all captured articles in detail, we will prioritize the selection of articles. Our criteria for prioritization will include the following: (1) unique or comprehensive insights are provided, (2) article is broadly applicable and generalizable, and (3) sufficient information is reported for extraction. We will also characterise and group the collected articles into those covering mainly processing issues and those covering more microbiological issues. This will enable the specialist knowledge of the project team to be applied to their best strengths when extracting and reviewing the literature in Objectives 3 and 4.

Objective 2 will produce a database consisting of collated citations and abstracts of (1) all articles identified in the literature search, and (2) screened articles considered of direct relevance to the overall objectives of the project. This database will also provide the criteria used for the selection and non-selection of relevant articles.

To realise **Objective 3**, **data extraction and analysis**, data from the articles identified, screened, and collated as relevant in Objective 2 will be extracted and analysed by the project team as per the following key approaches.

Data extraction and analysis of relevant literature

An in-depth content analysis of the selected articles will be carried out. For each article identified as relevant, two researchers will read the entire paper. Each will extract the key elements of interest from each paper. These will be collated by the PI and used to produce the draft critical review of the literature. The complied draft critical review will then be reviewed by the entire project team, with the final editing carried out by the PI before submission to the FSA Project Officer.

The reviewers will assess what existing data there is in the literature that addresses the following key questions/points:

- Is there evidence to show that heat completely destroys DNA (particularly AMR genes)?
- Can heat-treated or damaged DNA (AMR genes should be the focus) originating from dead bacteria be taken up by live bacteria?
- Does heat treatment of DNA and particularly AMR genes (including those on mobile genetic elements) affect its ability to be taken up by viable bacteria? Ideally this should be within a food context.
- Is there any information relating to transformation frequencies of heat treated/damaged DNA versus intact DNA? If so, is there a difference?
- What is the impact of different heat treatments on AMR gene uptake by viable bacteria? Literature will be considered on the effects of bacterial DNA (with a focus on AMR genes) exposure to different heat treatments and subsequent effects on uptake of this DNA by viable bacterial cells. Mobile genetic elements will also be considered. If the literature does not contain such detailed information (e.g. time/temperature combinations), any information obtained will be contextualised in terms of food e.g. cooking conditions where possible. Milder heat treatments such as low temperature sous vide, flash frying, slow cooker, rare or light cooking, etc will also be considered.
- Is there any evidence of uptake of heat damaged DNA and particularly AMR genes by pathogenic and non-pathogenic bacteria? If this evidence is not directly related to the food/gut environment it will be contextualised where possible. The review will focus on the resistance genes relating to Critically Important Antimicrobials (CIAs).
- Does the literature provide any indication that heat damaged DNA (AMR genes particularly) can be taken up by viable bacteria? If there is, is there any information to suggest that this can also occur in complex environments (e.g. in the presence of large, diverse microbial

communities such as the human gut, or complex media such as food (including combined foods) or on food contact materials or biofilms)?
- Is there any evidence to suggest that the behaviour of chromosomal DNA and plasmid DNA in response to heat differs?

As previously stated, a list of immediate and potential AMR genes of concern will be complied as the literature search and analysis progresses. The review will focus on critically important AMR genes, using the WHO list of critically important antimicrobials for human medicine (WHO, 2019) as a reference. It will initially focus on the highest priority classes of antimicrobials on the list and decide within those classes which antimicrobials and hence resistance genes to narrow down and focus on and provide a rational for the decisions. The approach will then consider the high priority classes of antimicrobials on this list and their resistance genes.

A template for data extraction will be prepared by the research team based on the PIO (Population, Intervention and Outcome(s)) as an Excel document (version 16, Microsoft Corp. Redmond, WA, USA). This template will be tested prior to implementation. Once implemented, the template will be used by reviewers to collect the data from eligible studies. Study characteristics (e.g., study design, sample size, sampling methods amongst others) and outcome(s) of interest will be described and summarised accordingly. A risk of bias assessment will be conducted after the data extraction process.

If any published studies are found that include quantifiable evidence on the impact of heat treatments on AMR genes, then the application of a basic scoring system to objectively quantify the robustness of the work will be considered and a risk of bias assessment will be conducted. The usefulness of such an approach will be discussed within the project team and with the Agency before being applied. Its application will in part depend on the number of articles that are found to have relevant quantifiable data. It is expected that most studies in this review will be deemed at a high risk of bias due to the lack of representativeness of data and lack of comparability of studies. If this approach is carried out then a mixed-method synthesis approach will be applied based on that used in previously published systematic reviews such as those by Thomas et al. (2012), Mateus et al. (2016), and FAO/WHO (2016). A basic scoring system will be used to objectively quantify the robustness of the work based on that outlined by Jadad & Murray (2007). And a modified version of the Cochrane Collaboration's Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach, as used by FAO/WHO (2016), will be used to classify the confidence in the impact of a secondary food processing activity.

Objective 3 will produce a database consisting of the key data extracted from articles of direct relevance to the overall objectives of the project.

To realise **Objective 4**, **Data synthesis and review completion**, the data extracted and analysed from individual articles in Objective 3 will be synthesised and reviewed by the project team and a formal technical report completed, as per the following key approaches.

Data synthesis and report completion

To synthesise the data extracted and evaluate its quality a narrative approach will be used. This will be used to; a) develop a synthesis of findings of the studies, b) investigate relationships within and between studies, and c), evaluate the degree of robustness of the synthesis. The findings of the review will be collected in a technical report. A database of the articles included in the review will also be provided. The database will be in a format suitable for publication on the FSA website. The technical report will identify the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria. The report will also highlight any information gaps and identify and recommend areas for further work.

A draft final report will be submitted at least 4 weeks before the final report is due to allow time for Agency officials to provide comments.

Objective 4 will produce a report that will include a lay summary, executive summary, introduction (including the background and aims/objectives of the study), methodology, and key findings of the review, discussions, conclusions, what remains unknown, uncertainty around findings, and recommendations for further work. The criteria for selection and non-selection of articles relevant for consideration in the review will also be clearly identified in the report.

To realise **Objective 5**, **Dissemination**, a full dissemination and exploitation plan will be agreed with the FSA Project Officer during the project.

Following completion of the final report, a meeting will be held with FSA officials after completion of the final report to discuss the key project findings and recommendations arising from the review. In addition to the final report the findings of the project will be disseminated to key stakeholders in the form of a scientific paper (with the approval of the funder) and presentations. Example dissemination activities may include:

1. An executive summary document / press release agreed with the Agency and distributed to key stakeholders.
2. At least one key paper will be submitted on "A comprehensive critical review of the impact of heat treatment on AMR bacteria/genes" for consideration for publication in a suitable peer-reviewed journal (such as Food Control or International Journal of Food Microbiology).
3. The presentation of results at any FSA conference, workshop, seminar or related event, as required by the Agency.
4. Presenting, or supporting the presentation, of the findings of this work at a future FSA AMR 'show and tell' event, ACMSF (or AMR sub-group) meetings, and at a stakeholder meetings, if needed.
5. Assisting the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on news story.

Timeframe: The proposed review will take 6 months to complete.

Key project outcomes

This proposed review will help increase the Agency's understanding of whether and to what extent AMR genes and mobile genetic elements (e.g. plasmids) from 'dead' bacteria in cooked foods can be taken up by 'live' bacteria in the human gut and other foods. It will:

1. Enable an understanding of which specific risks should be targeted to reduce the transmission pathway of AMR in humans and identify where the knowledge gaps for further interventions and research/surveillance are required. It will provide robust, evidence-based analysis of the impact of heat treatments (including cooking) on survival of AMR bacteria and AMR genes and make recommendations for any further work required.
2. Provide a review that will be used to inform measurable progress towards developing interventions and research/surveillance that will protect consumers from the risks associated with AMR and AMR genes.
3. Provide findings that will help the agency achieve its main aim of protecting public health from all potential risks which may arise in connection with the consumption of food.
4. Provide a report that will be used to inform Food Business Operators (FBOs) producers, food service operators, suppliers, and consumers, what realistic actions are required to reduce the risks associated with AMR and make a timely positive contribution to the cross-governmental objective of protecting consumers from the risks associated with AMR and AMR genes.

Key deliverables will be:

- A full technical report addressing the relevant areas of the study in a format suitable for publication on the Agency website. The report will include a lay summary, executive summary, introduction (including the background and aims/objectives of the research), methodology, findings, discussions (including the limitations of the models created), conclusions, references and recommendations for further work.
- Full details of the data collected will be provided in a systemised format and a library of references organised using an appropriate reference management system.
- Publication of research findings in peer reviewed open access literature and presentations at scientific conferences. Such material will be submitted to the Agency for approval prior to submission.

- A meeting with Agency officials to discuss the project findings and active support in subsequent dissemination of the findings.

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B. INNOVATION

Please provide details of any aspect of the proposed work which are considered innovative in design and/or application? E.g. Introduction of new or significant improved products, services, methods, processes, markets and forms of organization.

The approach taken by this project will be based on firm established methods for carrying out such a critical reviews of published literature. It will however differ in some respects from recent systematic reviews in not restricting the data reviewed to purely quantifiable data, since we believe that it is important to gain a thorough understanding of the current state of knowledge. We believe that opinion is equally import in this case, in order to gain a greater understanding of the role of heat treatments of food in reducing the transmission pathway of AMR in humans and to identify where the knowledge gaps for further interventions and where further research/surveillance is required.

We also believe it is very important that those carrying out this review have a good knowledge of heat-based technologies and methods, including cooking methods, that are used across the food industry, as well as by food service and domestically. This will ensure that the review is carried out in context. Within the research team there is extensive knowledge and understanding of thermal death kinetics and how this relates to heat processing and cooking operations, as well as microbiological and AMR knowledge. This knowledge and background of working within the food industry will ensure that the findings of this work can be used to inform food business operators (FBOs) producers, food service operators, suppliers, and consumers, of what realistic actions are required to reduce the risks associated with AMR. We feel that applying such a level of knowledge and experience to a review such as this is innovative and essential.

3: THE PROJECT PLAN AND DELIVERABLES

A. THE PLAN

Please provide a detailed project plan including, the tasks and sub-tasks required to realise the objectives (detailed in Part 1). The tasks should be numbered in the same way as the objectives and should be clearly linked to each of the objectives. Please also attach a flow chart illustrating the proposed plan.

The following work programme will commence on the 1st November 2020, as agreed with the Agency.

The project has been structured to look at the key interactions in a methodical but cost-effective manner. Work on some Objectives and Tasks will be carried out in parallel, using material produced in other Tasks.

It is proposed that the review question will be: "Do heat treatments applied to eliminate bacterial contamination in foods also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings, including the human gut and other foods?"

The key elements of the question (PIO): Population (P), Intervention (I), and Outcome (O) are:

- The **population** of interest include pathogenic and non-pathogenic AMR bacteria (such as *Acinetobacter baumannii*, *Campylobacter*, *Enterobacter*, *Enterococcus faecium* and *faecalis*, commensal *Escherichia coli*, *Klebsiella pneumoniae*, *Listeria*, *Salmonella*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* *) and specifically their AMR genes.
- Any heat treatment **interventions** applied to foods are considered relevant, such as pasteurisation, sterilisation, cooking treatments (e.g. hot air (oven), steam, hot water (boiling, blanching), hot fat or oil (shallow or deep frying), grilling, radiant, dielectric (microwave), extrusion, pressure, retort, etc.), and mild heat treatments (e.g. low temperature sous vide, flash frying, slow cooker, rare or light cooking, hot smoking, etc.)
- Relevant **outcome measures** for interventions are does the intervention induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings including the human gut and other foods.

* The search will not be restricted to this list alone, a full list of organisms will be agreed with the FSA Project Officer prior to commencing the literature search. Also if other microorganisms are identified during the course of the project we will consider adding these, following consultation with the FSA Project Officer.

All AMR genes of immediate or emerging concern will be considered. A search for specific AMR genes will not be carried out in the initial literature search, since there are so many of potential concern, some with rapid mechanisms for transfer. We intend to build a list of immediate and potential AMR genes of concern as the literature search and analysis progresses. The review will focus on critically important AMR genes, using the WHO list of critically important antimicrobials for human medicine (WHO, 2019) as a reference. We will initially focus on the highest priority classes of antimicrobials on the list and decide within those classes which antimicrobials and hence resistance genes to narrow down and focus on and provide a rational for the decisions. The approach will then consider the high priority classes of antimicrobials on this list and their resistance genes.

Objective 1: Literature search – Identification and collection of articles that may relevant data on the impact of heat treatment of food on AMR genes

Timescale: Months 1 to 2 (and a revisit in Months 5 to 6)

Staff: All of the project team.

Task 1.1: Agreement of review question, keywords, scope, and eligibility criteria (Month 1)

The review question, keywords, scope of search, and eligibility criteria will be agreed with the Agency following consultation, before commencing the literature search.

Task 1.2: Literature search (Months 1 to 2)

Searches of the bibliographic databases will be carried out, using keywords agreed with the Agency.

The following databases / search engines will be used:

- Web of Science from 1990-current
- MEDLINE from 1990-current
- PubMed.Net from 1990–current
- Google Scholar from 1990-current
- EMBASE from 1990-current

- CAB abstracts from 1990-current
- ScienceDirect from 1990-current
- Biomed Central from 1990-current
- Food Science and Technology abstracts from 1990-current

If any other relevant databases are identified in the early stages of the project, these will be considered and include if agreed of importance by the project team and FSA Project Officer.

In addition to the database searches, collation will be supplemented by:

- Searching through relevant government reports, e.g. FSA published studies, ACMSF reports, etc.
- European and International literature, e.g. EFSA scientific opinions, WHO reports, etc.
- Searching of key journals, e.g. International Journal of Food Microbiology, Journal of Food Protection, etc.
- Searching articles, e.g. Environmental Health News Magazine/Online.
- Contacting experts.
- Reference list tracking, Reference lists of all studies selected for inclusion will be searched to identify further relevant studies.
- A public “call for data”.

Finalised keywords will be agreed with the Agency prior to project initiation. A suggested search string is:

(“antimicrobial resistan*” OR “antibiotic resistan*” OR “antibacterial resistan*” OR multirestan* OR “multidrug resistan*” OR “multi-drug resistan*” OR “multiantibiotic resistan*” OR AMR OR MDR OR MAR OR AR OR AMRG) AND (Acinetobacter OR Campylobacter OR commensal OR Enterobacter OR Enterococcus OR “Escherichia coli” OR “E. coli” OR Klebsiella OR Listeria OR Salmonella OR Staphylococcus OR pathogen* OR Pseudomonas) AND (heat OR thermal OR pasteuri* OR sterili* OR UHT OR HTST OR “hot water” OR steam OR boil* OR blanch* OR oven OR roast* OR fry OR “hot fat” OR grill* OR broil* OR microwave* OR “pressure cook*” OR retort OR “sous vide” OR cook* OR inactive* OR consumption OR sublethal OR “human gut” OR intestin* OR “bacterial outer membrane vesicle*” OR OMV or biofilm* OR “extracellular polymeric saccharide*” OR EPS)

in Article title

OR

in Abstract

OR

in Subject headings

Any searches of the literature and criteria used will be documented at all times to allow replication of the methodology used.

To ensure that all of the pertinent papers are identified, the search strategy will be verified by checking the generated list of references against the cited reference lists of a random selection of five articles for all searches. To ensure completely random selection of articles, the papers will be sorted by author name and each assigned a sequential number. The formula =n * rand() will be used in Excel (version 16; Microsoft Corp. Redmond, WA, USA) to generate a list of random numbers corresponding to the papers. The ‘cited by’ functionality of the Web of Science will then be used to identify that articles published after the five randomly-selected references, which cited these papers, have been included in the search-generated reference list.

During this reviewing process individual authors or research teams carrying out very relevant work will be identified. These researchers will be contacted directly to ask whether they know of any other published or unpublished studies of direct relevance to the project.

Task 1.3: Collation of articles

For all searches, citations and abstracts will be uploaded from each of the electronic databases into Covidence [https://www.covidence.org]. The references will be processed using the ‘find duplicates’ automated functionality of the program and the duplicates will be removed.

Task 1.4: Revisit (Months 5 and 6)

In the penultimate month of the project the literature search will be performed again to identify if any new relevant articles have been published during the course of the project. Any papers identified will identified, screened, and reviewed in the same manner as previous articles, and if relevant incorporated into the final report.

Milestones and Deliverables:

M1: Before commencing the literature search, the review question, keywords, scope of search, and eligibility criteria will be agreed with the Agency (Task 1.1) at the first project meeting.

D1: Summary of initial results of literature database search - collated citations and abstracts (results of Task 1.3), submitted to Agency.

See Gantt and Deliverables table for further information.

Objective 2: Article screening – Selection of articles with relevant data on the impact of heat treatment of food on AMR genes

Timescale: Month 2

Staff: All of the project team.

Task 2.1: Selection of articles for data extraction

To ensure completely random selection of articles, the papers will be sorted by author name and each assigned a sequential number. The formula =n * rand() will be used in Excel (version 16; Microsoft Corp. Redmond, WA, USA) to generate a list of random numbers corresponding to the papers. The relevance of each unique citation will be assessed at the title and abstract level using an a priori developed form. The form will include one key question to determine the citation's relevance to the review question and eligibility criteria. Abstracts will be excluded if:

- They contain no relevant data on the impact of heat treatment on antimicrobial resistance genes that may be present in heat-killed foodborne bacteria and their potential uptake by other 'live' bacteria in the human gut and other foods.
- Are in a language other than English.
- Duplicate data.
- Measure irrelevant interventions (no heat treatment), outcomes, or populations or samples.

The criteria will be independently applied to the abstract of each paper by at least two members of the five member project team. For each citation, a consensus will be reached that the citation is relevant for inclusion. Arbitration by a third member of the project team will be used to settle conflicting appraisals. Full articles will be obtained for all abstracts that pass the inclusion criteria. To ensure transparency a record will be kept of all articles determined as not relevant.

Milestones and Deliverables:

M2: Initial literature search and screening completed (Objective 2 complete).

D2: Summary of screened database of relevant collated citations and abstracts (results of Task 2.1), submitted to Agency.

See Gantt and Deliverables table for further information.

Mid-point interim review (Month 3)

In Month 3 a short mid-point interim report will be produced for the Project Officer which will report on project progress across both Objectives and all Tasks.

Milestones and Deliverables:

D3: Mid-point interim project progress report submitted to Agency.

Objective 3: Data extraction and analysis - extraction of relevant data on the impact of heat treatment of food on AMR genes

Time scale: Months 2 to 4.

Staff: All of the project team.

Task 4.1: Data extraction from relevant articles and analysis

When extracting data from the individual screened articles, the reviewers will bear in mind the review question, i.e. “Do heat treatments applied to eliminate bacterial contamination in foods also induce sufficient damage to AMR genes to prevent their uptake by surrounding viable bacteria present in other settings, including the human gut?”

An in-depth content analysis of the selected articles will be carried out. For each article identified as relevant, two researchers will read the entire paper. Each will extract the key elements of interest from each article.

The reviewers will assess what existing data is there in the literature that addresses the following key questions/points:

- Is there evidence to show that heat completely destroys DNA (particularly AMR genes)?
- Can heat-treated or damaged DNA (AMR genes should be the focus) originating from dead bacteria be taken up by live bacteria?
- Does heat treatment of DNA and particularly AMR genes (including those on mobile genetic elements) affect its ability to be taken up by viable bacteria? Ideally this should be within a food context.
- Is there any information relating to transformation frequencies of heat treated/damaged DNA versus intact DNA? If so, is there a difference?
- What is the impact of different heat treatments on AMR gene uptake by viable bacteria? Literature will be considered on the effects of bacterial DNA (with a focus on AMR genes) exposure to different heat treatments and subsequent effects on uptake of this DNA by viable bacterial cells. Mobile genetic elements will also be considered. If the literature does not contain such detailed information (e.g. time/temperature combinations), any information obtained will be contextualised in terms of food e.g. cooking conditions where possible. Milder heat treatments such as low temperature sous vide, flash frying, slow cooker, rare or light cooking, etc will also be considered.
- Is there any evidence of uptake of heat damaged DNA and particularly AMR genes by pathogenic and non-pathogenic bacteria? If this evidence is not directly related to the food/gut environment it will be contextualised where possible. The review will focus on the resistance genes relating to Critically Important Antimicrobials (CIAs).
- Does the literature provide any indication that heat damaged DNA (AMR genes particularly) can be taken up by viable bacteria? If there is, is there any information to suggest that this can also occur in complex environments (e.g. in the presence of large, diverse microbial communities such as the human gut, or complex media such as food (including combined foods) or on food contact materials or biofilms)?
- Is there any evidence to suggest that the behaviour of chromosomal DNA and plasmid DNA in response to heat differs?
- Is there any evidence on the role of proteins in the transfer of AMR genes from AMR bacteria subjected to heat treatments?
- Is there any evidence on the role of outer membrane vesicles (OMVs) in the survival and transfer of AMR genes from AMR bacteria subjected to heat treatments?

As previously stated, a list of immediate and potential AMR genes of concern will be complied as the literature search and analysis progresses. The review will focus on critically important AMR genes, using the WHO list of critically important antimicrobials for human medicine (WHO, 2019) as a reference. It will initially focus on the highest priority classes of antimicrobials on the list and decide within those classes which antimicrobials and hence resistance genes to narrow down and focus on and provide a rational for the decisions. The approach will then consider the high priority classes of antimicrobials on this list and their resistance genes.

A template for data extraction will be prepared by the research team based on the PIO (Population, Intervention and Outcome(s)) as an Excel document (version 16, Microsoft Corp. Redmond, WA, USA). This template will be tested prior to implementation. Once implemented, the template will be used by reviewers to collect the data from eligible studies. Study characteristics (e.g., study design, sample size, sampling methods amongst others) and outcome(s) of interest will be described and

summarised accordingly. A risk of bias assessment will be conducted after the data extraction process.

If any published studies are found that include quantifiable evidence on the impact of heat treatments on AMR genes, then the application of a basic scoring system to objectively quantify the robustness of the work will be considered. The usefulness of such an approach will be discussed within the project team and with the Agency before being applied. Its application will in part depend on the number of articles that are found to have relevant quantifiable data. If this approach is carried out then a mixed-method synthesis approach will be applied based on that used in previously published systematic reviews such as those by Thomas et al. (2012), Mateus et al. (2016), and FAO/WHO (2016). A basic scoring system will be used to objectively quantify the robustness of the work based on that outlined by Jadad & Murray (2007). And a modified version of the Cochrane Collaboration's Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach, as used by FAO/WHO (2016), will be used to classify the confidence in the impact of a secondary food processing activity.

Deliverables:

M3: Data extraction and analysis of articles completed (Task 3.1 complete).

Objective 4: Data synthesis and report completion – review of published literature on the impact of heat treatment of food on AMR genes

Timescale: Months 5 to 6

Staff: All of the project team.

To synthesise the data extracted and evaluate its quality a narrative approach will be used. This will be used to; a) develop a preliminary synthesis of findings of the integrated studies, b) investigate relationships within and between studies, and c), evaluate the degree of robustness of the synthesis. The findings of the review will be collected in a technical report. A database of the articles included in the review will also be provided. The database will be in a format suitable for publication on the FSA website. The technical report will identify the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria. The report will also highlight any information gaps and identify and recommend areas for further work.

The report will include a lay summary, executive summary, introduction (including the background and aims/objectives of the study), methodology, and key findings of the review, discussions, conclusions, what remains unknown, uncertainty around findings, and recommendations for further work. The criteria for selection and non-selection of articles relevant for consideration in the review will also be clearly identified in the report.

Task 4.1: Write up draft final report (Month 5)

A draft final report will be submitted at least 4 weeks before the final report is due to allow time for Agency officials to provide comments.

Task 4.2: Write up final report (Month 6)

Following consultation with the Agency after completion of the draft final report, a final report will be produced.

Deliverables:

M4: Project completed (Objective 4 complete)

D4: Draft of the final report (Task 4.1 complete) submitted to Agency

D5: Final report (Task 4.2 complete), including database of articles included in the review, submitted to Agency

Objective 5: Dissemination

Timescale: Month 6 and beyond

Staff: All of the project team.

A full dissemination and exploitation plan will be agreed with the FSA Project Officer during the project. A meeting will be held with FSA officials after completion of the final report to discuss the key project findings and recommendations arising from the review (Task 5.1).

In addition to the final report the findings of the project will be disseminated to key stakeholders in the form of a scientific paper (with the approval of the funder) and presentations. Example dissemination activities may include:

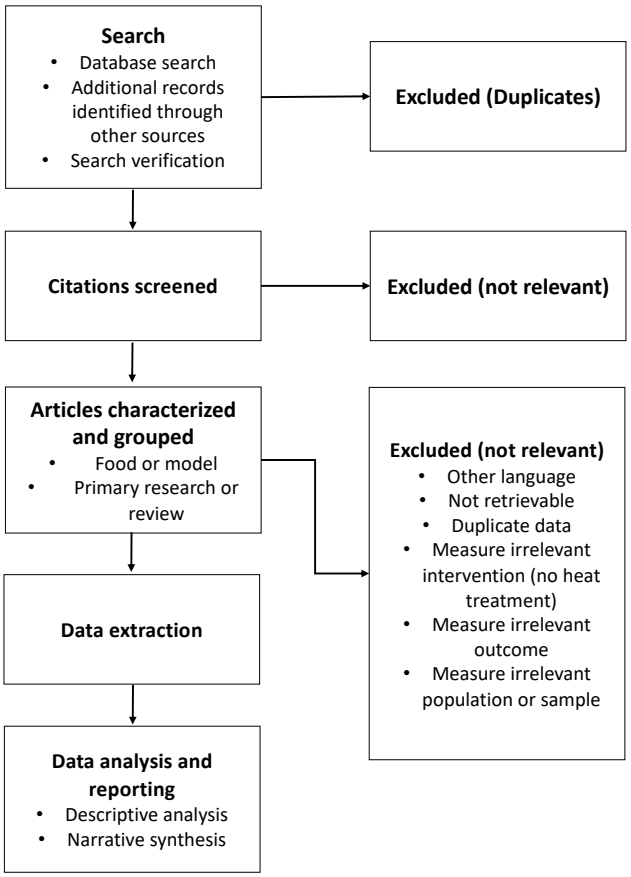
1. An executive summary document / press release agreed with the Agency and distributed to key stakeholders.
2. At least one key paper will be submitted on “A comprehensive critical review of the impact of heat treatment on AMR bacteria/genes” for consideration for publication in a suitable peer-reviewed journal (such as Food Control or International Journal of Food Microbiology).
3. The presentation of results at any FSA conference, workshop, seminar or related event, as required.
4. Presenting, or supporting the presentation, of the findings of this work at a future FSA AMR ‘show and tell’ event, ACMSF (or AMR sub-group) meetings, and at a stakeholder meetings, if needed.
5. Assisting the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on news story.

Deliverables:

D6: Meeting with FSA officials to discuss key findings and recommendations arising from the review.

See Gantt and Deliverables table for further information.

A flow chart of the knowledge synthesis process for this review is shown below:



The Gantt chart below sets out the work timetable for this proposed project:

	Project Year / Month						
	Nov 20 (month 1)	**Dec 20 (month 2)**	**Jan 21 (month 3)**	**Feb 21 (month 4)**	**Mar 21 (month 5)**	**Apr 21 (month 6)**	**May 21 (month 7)**
Objective 1: Literature search							
Task 1.1: Agreement of review question, keywords, scope, and eligibility criteria							
Task 1.2: Literature search							
Task 1.3: Collation of articles							
Task 1.4: Revisit							
Objective 2: Article screening							
Task 2.1: Selection of articles for data extraction							
Mid-point interim review							
Objective 3: Data extraction and analysis							

Task 3.1: Data extraction from relevant articles and analysis							
Objective 4: Data synthesis and report completion							
Task 4.1: Write up draft final report							
Task 4.2: Write up final report							
Objective 5: Dissemination							
Task 5.1: Meeting with Agency							
Milestones	M1		M2	M3		M4	
Deliverables		D1	D2, D3		D4	D5	D6

B. DELIVERABLES

Please outline the proposed project milestones and deliverables. Please provide a timetable of key dates or significant events for the project (for example fieldwork dates, dates for provision of research materials, draft and final reporting). Deliverables must be linked to the objectives.
For larger or more complex projects please insert as many deliverables /milestones as required.
Each deliverable should be:

i. no more 100 characters in length
ii. self-explanatory
iii. cross referenced with objective numbers i.e. deliverables for Objective 1 01/01, 01/02 Objective 2 02/01, 02/02 etc

Please insert additional rows to the table below as required.

A final deliverable pertaining to a retention fee of 20 % of the total value of the prosed work will automatically be calculated on the financial template.

DELIVERABLE NUMBER OR MILESTONE IN ORDER OF EXPECTED ACHIEVEMENT	TARGET DATE	TITLE OF DELIVERABLE OR MILESTONE
M1	**06/11/2020**	**First project meeting (Task 1.1)**
D1 (1/1)	**19/12/2020**	**Provide a summary of initial results of literature database search (Task 1.3) to the FSA**
D2 (2/1)	**05/01/2021**	**Provide summary of screened database of relevant collated citations and abstracts (Task 2.1) to the FSA**
M2	**05/01/2021**	**Initial literature search and screening completed (Objectives 1 and 2 complete)**
D3	**22/01/2021**	**Submit a mid-point interim report on progress on Objectives 1, 2, and 3 to the FSA**
M3	**26/02/2021**	**Data extraction and analysis of individual articles completed (Objective 3 complete)**
D4 (4/1)	**30/03/2021**	**Submit draft of the final report (Task 4.1) to the FSA**
D5 (4/2)	**29/04/2021**	**Submit final report (Task 4.2) to the FSA**
M4	**29/04/2021**	**Project completed (All objectives and tasks complete)**
D6 (5/1)	**28/05/2021**	**Meeting with FSA officials to discuss project findings (Task 5.1)**

4: ORGANISATIONAL EXPERIENCE, EXPERTISE and STAFF EFFORT

A. PARTICIPATING ORGANISATIONS' PAST PERFORMANCE

Please provide evidence of up to three similar projects that the project lead applicant and/or members of the project team are currently undertaking or have recently completed. Please include:

- The start date (and if applicable) the end date of the project/(s)
- Name of the client who commissioned the project?
- Details of any collaborative partners and their contribution
- The value
- A brief description of the work carried out.
- How the example(s) demonstrate the relevant skills and/or expertise.
- What skills the team used to ensure the project (s) were successfully delivered.

The staff at FRPERC (Grimsby Institute) and the University of Lincoln who will be working on this project have extensive experience of having worked on numerous similar Agency projects on control measures and interventions to reduce pathogenic contamination during the processing of red meat, poultry, fish and other foods (including MAFF MH0211; MAFF MH0227 (FSA M01007); FSA M01019; FSA ZM0104; FSA M01039; FSA M01038; FSA M01054; FSAS FS241055; FSA FS503001; FSA FS203002**;** FSA FS101044; FSA FS514103, FSA FS102128, FSA 101193). The following are three similar projects that they have recently completed:

FSA SEP-EOI-02: Exploration of the potential for technology to support agency objectives in meat operations
Date: 2016-2017 (9 months)
Client: Food Standards Agency
Partners: Grimsby Institute, FRPERC; University of Lincoln, NCFM
Value: £57,691.60
Description of work: The aim of this desk-based project was to explore the development a science-based approach to evaluate the effectiveness of automated surveillance and inspection procedures in meat production, focusing primarily on the implications for public health. The study addressed three, fundamental, risk assessment questions: (1) What are the real public health issues associated with meat produced under modern commercial conditions? (2) What current inspection/testing/monitoring techniques can be used to detect the factors controlling meat safety? (3) What alternative techniques could be used or developed?
To accomplish this, it had 4 objectives: (1) To critically review current science and commercially available inspection technologies; (2) To carry out a screening of potential inspection technologies; (3) To carry out a gap analysis and postulation of alternative surveillance protocols; (4) To disseminate the projects key findings and engage with industry (via seminar workshop towards the end of the project). This work showed that most of the meat animals' conditions of concern to human health that are assessed through current OV inspection practices, could be addressed by existing automated inspection techniques or possibly addressed by existing techniques after further development. The few conditions where no clear solution appeared to be available were (1) the PM detection of contamination with hair, (2) the AM detection of suspect residues in animals, and (3) Endocarditis in pig carcasses. These tasks present large challenges that need to be addressed by further research to develop potential technologies for their detection. A number of key techniques that we considered to be currently sufficiently advanced and the most promising for detection of specific conditions were recommend for further development.
How the example(s) demonstrate the relevant skills and/or expertise: This project demonstrates: the ability of the proposers to work together as a team on Agency projects; the ability of the team to horizon scan, search, collect, and critically review research literature on diverse but related subjects; the ability of the team to apply critical thinking and problem solving to research objectives; interaction and engagement with stakeholders and FBOs; the ability to keep to deadlines and achieve the desired deliverables on time and within budget.
What skills the team used to ensure the project (s) were successfully delivered: Literature searching and critical review; Teamwork; Opinion gathering from meat industry in UK; Building good working relationships with key stakeholders (UK meat processors and stake holder organisations (BMPA, BPC, and AIMS); Effective communication with stakeholders.

FSA FS514103: Microbial evaluation of poultry and pork mechanically separated meat (MSM), compared to fresh cuts of meat, meat preparations and minced meat products
Date: 2014-2016 (24 months)
Client: Food Standards Agency
Partners: Grimsby Institute, FRPERC; University of Lincoln, NCFM; Leatherhead Food RA
Value: £313,189.79
Description of work: This project provided data and evidence to inform the Agency of the microbial safety of mechanically separated meat (MSM) from poultry and pork. The outcomes were used to support the Agency's assessment of whether current restrictions on the use of MSM are appropriate and proportionate for the protection of the consumer. The project built on a previous research project carried out by the proposers and commissioned by the Agency entitled "Description of the processes used in the UK to manufacture MSM and former DSM meat products from poultry and pork and an initial assessment of microbiological risk".
How the example(s) demonstrate the relevant skills and/or expertise: This project demonstrates: the ability of the proposers to work together as a team on Agency projects; the ability of the team to apply critical thinking and problem solving to research objectives; to interact and engage with stakeholders and FBOs; the ability to keep to deadlines and achieve the desired deliverables on time and within budget.
What skills the team used to ensure the project (s) were successfully delivered: Literature searching and review; Teamwork; Data gathering from meat industry in UK; Building good working relationships with UK meat processors; Building good working relationships with key UK stakeholder organisations (BMPA, BPC, and AIMS); Effective communication with stakeholders.

FSA FS101044: Qualitative Risk Assessment to support a policy decision on partially eviscerated (effilé) poultry
Date: 2013-2014 (8 months)
Client: Food Standards Agency
Partners: Grimsby Institute, FRPERC; University of Lincoln, NCFM
Value: £104,191.00
Description of work: The overall aim of this project was to carry out a risk assessment of partially-eviscerated (effilé) poultry production (poultry with the heart, liver, kidneys, crop, proventriculus and gizzard left inside the body cavity) with a view to considering whether the risks of partially-eviscerated poultry production could be managed to an acceptable level such that the practice could be authorised in the UK. The approach involved obtaining and interpreting information from scientific literature and carrying out an initial risk assessment of the public health implications of allowing partially-eviscerated birds into the food chain together with a review of all relevant and appropriate literature/company information relating to the control of partially-eviscerated poultry production. An industrial survey of current production of partially-eviscerated poultry in France was also carried out. A series of short practical evaluations were also carried out for processes where further data was required. From this information, an assessment and comparison of the microbiological risks associated with the different production stages was implemented. Commentary was provided on the appropriateness of the required controls and restrictions for each stage of meat product production, and required changes/improvements were suggested. Finally, the identification of information gaps was carried out and recommendations made to the Agency.
How the example(s) demonstrate the relevant skills and/or expertise: This project demonstrates: the ability of the proposers to work together as a team on Agency projects; the ability of the team to apply critical thinking and problem solving to research objectives; interaction and engagement with stakeholders and FBOs; adherence to deadlines and achievement the desired deliverables on time and within budget.
What skills the team used to ensure the project (s) were successfully delivered: Teamwork; Data gathering from meat industry in UK and abroad; Critical re-evaluations of meat inspection protocols; Microbial risk & Hazard assessment; Effective communicating with stakeholders; Design and performance of targeted practical experiments.

B. NAMED STAFF MEMBERS AND DETAILS OF THEIR SPECIALISM AND EXPERTISE

For each participating organisation on the project team please list:- the names and grades of all staff who will work on the project together with details of their specialism and expertise, their role in the project and details of up to 4 of

their most recent, relevant published peer reviewed papers (where applicable). If new staff will be hired to deliver the project, please detail their grade, area/(s) of specialism and their role in the project team.

Lead Applicant	TEC Partnership, Grimsby Institute of Further & Higher Education, Food Refrigeration and Process Engineering Research Centre (FRPERC)

Named staff members, details of specialism and expertise.

An experienced team of food process engineers from the Grimsby Institute's Food Refrigeration & Process Engineering Research Centre (FRPERC) will be carrying out the proposed project. The main effort will be carried out by the Principal Investigator Christian James, with the support of Research Assistant Luke Talbot and FRPERC Director (Emeritus) Stephen James. They are all experienced at carrying out critical literature reviews on many aspects of food, including meat, processing, including the impact of processing steps on the contamination and spread of microbial contamination. All also have practical experience of meat processing, from farm-to-fork, including optimising meat processing unit operations and analysis of the impact that different meat processing operations have on the presence, spread, and control of microbial and physical contamination. They also have practical experience of applying a wide variety of interventions (both physical and chemical) for meats (red meat and poultry) and other foods, at all stages along the production chain, from lairage to consumption. They have been lead authors/co-authors of the following reviews (or projects including reviews of literature) for the Agency:

James, C. & James, S. J. (1995) Past and future research into methods of red meat decontamination. MAFF contract MH0211.

James, C., Nicolaon, M. & James, S. J. (1999) Review of microbial contamination and control measures in abattoirs. MAFF contract MH0227 (FSA MO1007).

James, C., Purnell, G. & James, S. J. (2003) Review of the use of ozone in red meat and poultry processing. Food Standards Agency (FSA) project no. ZM0104.

James, C., James, S. J. & Buncic, S. (2004) Review of potential effects of transporting meat above 7°C. Food Standards Agency (FSA) project no. ZM01011.

James, C., Pinho, R. M. & James, S. J. (2006) Safety implications of the manufacture of minced meat from aged meat. Food Standards Agency (FSA), FRPERC project number 2006141.

Corry, J., Allen, V., Whyte, R., Tinker, D., James, C., Purnell, G. & James, S. J. (2007) Physical methods readily adapted to existing commercial lines for reducing pathogens, particularly campylobacters, on raw poultry. Food Standards Agency (FSA) project no. MO1019.

Newell, D. G., Allen, V., Elvers, K., Dorfper, D., Hanssen, I, Jones, P., James, S., Gittins, J., Stern, N., Davies, R., Connerton, I., Pearson, D. & Salvat, G. (2008) B15025: A critical review of interventions and strategies (both biosecurity and non-biosecurity) to reduce Campylobacter on the poultry farm. Food Standards Agency (FSA) project no. B15025.

James, C., Wilkin, C.-A., Purnell, G. & James, S. J. (2009) Reduction of salmonella contamination of pig meat. Food Standards Agency (FSA) project no. MO1038.

James, C. & James, S. J. (2012) Quantification of the controls that should be placed on meat prior to mincing. Food Standards Agency (FSA) project no. MO1054.

James, C., Purnell, G. & James, S. J. (2013) Description of the processes used in the UK to manufacture MSM and former DSM meat products from poultry and pork and an initial assessment of microbiological risk. Food Standards Agency (FSA) project no. FS503001.

James, C., Derrick, S., Purnell, G. & James, S. J. (2013) Review of the risk management practices employed throughout the fish processing chain in relation to controlling histamine formation in at-risk fish species. Food Standards Agency (FSA) project no. FS241055.

James, C., Daramola, B., Dudkiewicz, A., Reyers, F., Purnell, G., Turner, R., James, S. J. & Braybrooks, V. (2014) Qualitative Risk Assessment to support a policy decision on partially-eviscerated (effilé) poultry production. Food Standards Agency (FSA) project no. FS101044.

James, C., Daramola, B., Chu, J., Dudkiewicz, A., Purnell, G. & James, S. J. (2018) Exploring the potential for technology to support agency objectives in meat operations. Food Standards Agency (FSA) project no. SEP-EOI-02. In Press.

FRPERC are a department of the Grimsby Institute of Further & Higher Education. They have a long track record of providing high quality research for UK and International funders. This has resulted in over 900 scientific publications in their 50 year history. The group was originally part of the Meat Research Institute founded in 1967 (later the Institute of Food Research – Bristol Laboratory), before becoming a Research Centre at the University of Bristol for 18 years before moving to the Grimsby Institute of Further & Higher Education (GIFHE) in 2009. Between them the research staff who will be working on this project have extensive experience of having worked on 19 Agency funded studies since 2000 on reducing the spread of microbial contamination during the processing of foods of animal origin. Their consultancy for the food industry has included data gathering exercises and optimisation of chilling and freezing operations, product quality, energy, and staff training (on temperature control, food safety, etc).

Christian James, BSc (Hons) Food Technology, MIFST, is a Senior Research Fellow at FRPERC.

Christian is a Food Technology graduate. Since joining FRPERC in 1993, his work has covered many different aspects of food processing including: heat and mass transfer in foods during heating and cooling, microwave processing and the decontamination of meat, fish and vegetables, with over 150 publications in these areas. His first project at FRPERC was to carry out a review of meat interventions for MAFF. Much of his recent work has been on the topics of food contamination/decontamination and food refrigeration. He has extensive experience of performing such tasks for previous MAFF/FSA projects (MAFF MH0211: Past and future research into methods of red meat decontamination; MAFF MH0227 (FSA M01007): Review of microbial contamination and control measures in abattoirs; FSA M01019: Physical methods readily adapted to existing commercial lines for reducing pathogens, particularly Campylobacters, on raw poultry; FSA ZM0104: Review of the use of ozone in red meat and poultry processing; FSA M01039: Reducing Campylobacter cross-contamination during poultry processing; FSA M01038: Reduction of salmonella contamination of pig meat; FSA project M01054: Quantification of the controls that should be placed on meat prior to mincing; FSAS FS241055: Review of the risk management practices employed throughout the fish processing chain in relation to controlling histamine formation in at-risk fish species in Scotland; FSA FS503001: Description of the processes used in the UK to manufacture MSM and former DSM meat products from poultry and pork and an initial assessment of microbiological risk; FSA SEP-EOI-02: Exploration of the potential for technology to support agency objectives in meat operations).

He is a Visiting Senior Fellow at the University of Lincoln, a Member of the Institute of Food Science and Technology (UK), a Member of the Editorial Board of Food and Bioprocess Technology: An International Journal, has also been on EFSA Bio-Hazard working groups, and is listed on the European Food Safety Authority's (EFSA) Food Safety Experts Database. He is also currently a member of Working Group 3 of the COST Action "Risk- based meat inspection and integrated meat safety assurance" (RIBMINS) CA18105 where he is a member of the group reviewing the role of unit operations and intervention methods in reducing microbial risks on poultry at the abattoir. Literature pertinent to this project had been collated and is currently being reviewed within the COST project.

Four publications:

1. James, C., James, S. J., Hannay, N., Purnell, G., Barbedo-Pinto, C. S., Yaman, H., Araujo, M., Gonzalez, M. L., Calvo, J., Howell, M., & Corry, J. E. L. (2007). Decontamination of poultry carcasses using steam or hot water in combination with rapid cooling, chilling or freezing of carcass surfaces. *International Journal of Food Microbiology*, 114, 195-203.
2. Purnell, G., & James, C. (2012). Advances in food surface pasteurization by thermal methods. Chpt 8, 241-273. *Microbial Decontamination in the Food Industry: Novel Methods and Applications*, edited by Demirci, A. & Ngadi, M. O.. Woodhead Publishing Ltd.
3. Hamidi-Oskouei, A. M., James, C., & James, S. (2015). The efficiency of UVC radiation in the inactivation of Listeria monocytogenes on beef-agar food models. *Food Technology and Biotechnology*, 53:3, 231-236.
4. James, C., Onarinde, B. A., & James, S. J. (2017). The use and performance of household refrigerators: A review. *Comprehensive Reviews in Food Science and Food Safety*, 16(1), 160–179.

Luke Talbot, BSc (Hons) Natural Sciences with Biology and Anthropology, is a Research Assistant at FRPERC

Luke is a young, next generation researcher who has been working at FPRERC for three years across various projects on different aspects of food processing, including long term Innovate UK funded work and quick consultancy work for Industrial clients. This has included both desk-based study (including horizon scanning and literature searching/reviewing) and practical laboratory and in-field trials. In one recent Innovate UK funded project he monitored air and product temperatures in retail display units in the stores of a major UK retailer and used Combase and other microbial models to predict the impact of temperatures on microbial growth/survival.

- Talbot, L., Purnell, G., James, S. J., & James, C. (2020) Operating temperatures of supermarket frozen retail display cabinets. *International Journal of Refrigeration*. Vol. 117, pp81-93.

Stephen James, BA (Hons), is Director (Emeritus) of FRPERC. (His input will be in kind and not charged to the project.)

Stephen is a Mathematics graduate but has become a Food Engineer by experience. Since joining the Meat Research Institute in 1967, his work has covered all aspects of the production of meat and meat products, heat and mass transfer in foods, microwave processing and the decontamination of meat and vegetables, with over 450 publications in these areas. He is an Internationally recognised expert on all aspects of the food cold-chain from primary chilling/freezing to distribution, retail, catering and domestic handling and has written extensively on these subjects. Interests in food hygiene have developed from lamb cleaning in 1968 (as a replacement for the "wiping cloth") to leading a large EU funded project on the modelling of thermal destruction on microorganisms (BUGDEATH). He has managed the engineering input in four meat hygiene-orientated research projects funded by the FSA: M01039: Reducing campylobacter cross-contamination during poultry processing; M01038: Reduction of salmonella contamination of pig meat; M01046: Pre-skinning treatments of slaughtered cattle and sheep to improve meat safety; and B15025A critical review of interventions and strategies (both biosecurity and non-biosecurity) to reduce Campylobacter on the poultry farm. He was also project leader of a large Defra project ACO403: Fostering the development of technologies and practices to reduce the energy inputs into the refrigeration of food. He recently worked on FSA project M01054: Quantification of the controls that should be placed on meat prior to mincing, FSA FS101044: Qualitative Risk Assessment to support a policy decision on partially eviscerated (effilé) poultry production project, FS514103: Microbial evaluation of poultry and pork mechanically separated meat (MSM), compared to fresh cuts of meat, meat preparations and minced meat products, and FSA SEP-EOI-02: Exploration of the potential for technology to support agency objectives in meat operations. His consultancy for the food industry has included data gathering exercises and optimisation of chilling and freezing operations, product quality, energy, and staff training (on temperature control, food safety, etc).

He is a Visiting Senior Fellow at the University of Lincoln, and member of the International Advisory Board of the International Journal of Refrigeration; former member of the Institute of Refrigeration (IoR) and International Institute of Refrigeration (IIR), and former food editor of the International Journal of Refrigeration.

Four publications:

1. James, S. J., & Evans, J. A. (2006). Predicting the reduction in microbes on the surface of foods during surface pasteurisation – the 'BUGDEATH' project. *Journal of Food Engineering*, 76, 1-6.
2. Newell, D. G., Elvers, K. T., Dopfer, D. Hansson, I., Jones, P., James, S., Gittins, J., Stern, N. J., Davies, R., Connerton, I., Pearson, D., Salvat, G., & Allen, V. M. (2011). Biosecurity-based interventions and strategies to reduce Campylobacter spp. on poultry farms. *Applied and Environmental Microbiology*, 77, 8605-8614.
3. James, S. J. & James, C. (2014). Cooking of meat: Heat processing methods. 2nd Ed, 1, 385-390. *Encyclopedia of Meat Sciences* edited by Devine, C. & Dikeman, M. Academic Press, Elsevier Science Ltd.
4. James, C., Derrick, S., Purnell, G. & James, S.J. (2015). Histamine control in at-risk fish species in the Scottish fish processing chain. 2015 World Seafood Conference, 5-9th September 2015, Grimsby, UK.

Andy Goudie, Executive Director of Projects and Partnerships, will maintain oversight and take overall responsibility for the successful delivery of this project. He will report on project performance to the Institute's Senior Management Team and Corporation via the Executive Director, providing assurance that project activities will be scrutinised at the highest level. His input will be in kind and not charged to the project.

He has led and supported the development of externally funded education, training and research projects for over 21 years. He has extensive experience in managing budgets and external relationships, achieving sector-leading project performance.

External AMR consultant/expert

Professor Nicola Williams. Professor of Bacteria Zoonotic Disease at the University of Liverpool.

Nicola has expertise with both AMR and food-borne pathogens. She is a microbiologist with research interests including reservoirs and transmission of food-borne pathogens, transfer and maintenance of antimicrobial resistance, antimicrobial prescribing practice and the molecular epidemiology AMR bacteria in wildlife, livestock and companion animals. She has research experience on bacterial zoonoses (including antimicrobial resistance) in wildlife, food and companion animal species, investigating reservoirs, survival in the environment, fitness and transmission between animals and to humans, using a combination of conventional microbiology and molecular biology and next generation sequencing. She has a large portfolio of research on foodborne pathogens, antimicrobial use and resistance (£>5 million to date), and has funding from UK research councils, the UK Food Standards Agency and Department for Environment, Food, and Rural Affairs (Defra), industry (pharmaceutical, poultry producers, retailers) and EU (FP7 & EMIDA). Through her work she actively collaborates with colleagues in 10 EU countries, as well as Thailand, Kenya, Nigeria, Ethiopia and the US. She has published over 50 papers in peer-reviewed journals, many of which are on bacterial zoonoses, antimicrobial use and antimicrobial resistance.

Four publications:

1. Haldenby, S., Bronowski, C., Nelson, C., Kenny, J., Martinez-Rodriguez, C., Chaudhuri, R., **Williams, N. J.**, Forbes, K., Strachan, N. J., Pulman, J., Winstanley, I. N., Coreless, C. E. & Winstanley, I. N. (2020). Increasing prevalence of a fluoroquinolone resistance mutation amongst Campylobacter jejuni isolates from four human infectious intestinal disease studies in the United Kingdom. *Plos one*, 15(1), e0227535.
2. Hassell, J. M., Ward, M. J., Muloi, D., Bettridge, J. M., Robinson, T. P., Kariuki, S., Ogendo, A., Kiiru, J., Imboma, T., Kang'ethe, E. K., Oghren, E. M., **Williams, N. J**., Begon, M., Woodhouse, M. E. J., & Fèvre, E. M. (2019). Clinically relevant antimicrobial resistance at the wildlife–livestock–human interface in Nairobi: an epidemiological study. *The Lancet Planetary Health*, 3(6), e259-e269.
3. Schmidt, V., Pinchbeck, V., McIntyre, M., Nuttall, N., McEwan, N., Dawson, S. & **Williams, N. J.** (2018). Routine antibiotic therapy in dogs increases the detection of antimicrobial resistant faecal *Escherichia coli*. *J. Antimicrob. Chemother.* Accepted
4. Bortolami, A.**, Williams, N. J.,** *et al*. (2017). Environmental surveillance identifies multiple introductions of MRSA CC398 in an Equine Veterinary Hospital in the UK, 2011-2016. *Sci. Reps.* 7 (1):5499.

Participant Organisation 1	University of Lincoln

Named staff members, details of specialism and expertise.

The National Centre for Food Manufacturing (NCFM), the University of Lincoln's Holbeach Campus, based in South Lincolnshire, provides a national resource to agri-food businesses across the full range of their activities. The NCFM has outstanding sector-focused facilities, with provision shaped and dictated by the companies whose businesses the campus supports. The NCFM conducts industry based research and works with businesses upon bespoke projects in order to address specific food industry needs and issues. The NCFM has experience of providing high quality research funded by the KTPs (Knowledge Transfer Partnership), IUK (INNOVATE UK), and ESA

The School of Life Sciences (SLS) is based at the University of Lincoln's Brayford campus is based in Lincoln, Lincolnshire. The SLS is a rapidly expanding, international collection of researchers working at the forefront of disciplines across the breadth of the life sciences. The School has recently moved into the new Joseph Banks Laboratories, as part of a multimillion pound investment in research facilities and infrastructure to sustain and support our continued growth, including the creation of the Research and Enterprise hub of the University's new Science and Innovation Park. Research in the School is organised around four main themes, although collaboration and cross-disciplinary research between these groups occurs at all levels: 1) Animal Behaviour, Cognition and Welfare, 2) Drug Design and Delivery, 3) Evolution and Ecology and 4) Microbiology and Biotechnology.

MICROBIOLOGIST

Dr Bukola Onarinde, PhD Food Microbiology, MSc Food Science and Technology, BSc Microbiology, is an Associate Professor at the NCFM.

Bukola has very strong background in microbiology and has over 10 years of experience in conducting research involving microbial decontamination of foods using thermal and non-thermal processes such as bacteriophages, dry heat, moist heat, radio frequency and UV for decontaminating naturally contaminated and artificially inoculated foods in both laboratory and industrial settings. Bukola has for the past 3 years conducted process validation for food industry and food process manufacturers. At NCFM Bukola's role also involves managing research project conducted in collaboration with food industries (including Innovate UK projects). Her most recent FSA funded research projects are as follows: "Microbial evaluation of poultry and pork mechanically separated meat (MSM), compared to fresh cuts of meat, meat preparations and minced meat products." - FS514103; "Exploring the Potential for Technology to Support Agency Objectives in Meat Operations." - SEP-EOI-02 and "Qualitative Risk Assessment to support a policy decision on partially eviscerated (effilé) poultry production project" - FSA FS101044. Bukola has over the years developed an interest in AMR studies in food organisms and has such conducted few summer project funded internally by the department, one of such project as resulted in submission of a letter to the editor of Journal of Global Antimicrobial Resistance (JGAR) titled *Antimicrobial resistance pattern of Lactic Acid Bacteria (LAB) isolated from European fermented meat products purchased in Lincolnshire*. other studies include AMR study of commensals and pathogens associated with fresh pork meat.

Publications

1. Dudkiewicz, A., Masmejean, L., Arnaud, C., Onarinde, B., Sundara, R., Anvarian, A., & Tucker, N. (2020). Approaches for improvement in digestive survival of probiotics, a comparative study. *Polish Journal of Food and Nutrition Sciences*. ISSN 1230-0322
2. Onarinde, B., Zhao, J., Leonard, J., & Dudkiewicz, A (2019). Antimicrobial Resistance (AMR) Profiles of Lactic Acid Bacteria (LAB) Isolated from Fermented Meat Products of European Origin. In: *IAFP'S European Symposium on Food Safety*, 24 - 26 April, 2019, Nantes, France.
3. Onarinde, B. A., & Dixon, R. A. (2018). Prospects for Biocontrol of *Vibrio parahaemolyticus* Contamination in Blue Mussels (*Mytilus edulus*)—A Year-Long Study. *Frontiers in Microbiology*, 9:1043. doi:10.3389/fmicb.2018.01043.
4. James, C., Daramola, B., Dudkiewicz, A., Reyers, F., Purnell, G., Turner, R., James, S. J., & Braybrooks, V. (2014). *Qualitative Risk Assessment to support a policy decision on partially eviscerated (effilé) poultry production*. FSA Project report 2014.

ANTIMICROBIAL RESISTANCE EXPERT

Dr Ron Dixon, FRSB is a Reader in the School of Life Sciences, University of Lincoln.

He has extensive experience of human pathogen analysis and antibiotic resistance work in both animal and human studies. He has worked for 10 years in pharmaceutical research developing key antibiotics on the market today. He has worked in an academic environment for 30 years and currently has 5 PhDs and a PDRA engaged in the identification and containment of antibiotic resistance in farm animals and the environment. He is the academic partner (PI) for a £1.5m InnovateUK project funded by DHSC/GAMRIF to Arden Biotechnology (2019-2021) to develop the 'Biocontrol to combat *Clostridium perfringens* in poultry flocks (610335)'. He has sustained a forty-year interest in pharmaceutical biotechnology involving elucidating the mode of action of Veterinary antimicrobial

agents from both an industrial and academic perspective, developing projects to study the detailed molecular interactions of the antibacterial peptides and other agents with the bacterial envelope. He has supervised over 20 PhD candidates and several food animal-related KTP awards. Recently he has gained support to develop bacteriophages (phagebiotics) as part of an initiative in commercial poultry to reduce the emergence of AMR following the reduction of antibiotic growth promoters and develop a technical platform for other industrial applications.

Publications

1. Shaw, A. G., Cornwell, E., Sim, K., Thrower, H., Scott, H., Brown, J., **Dixon, R. A.**, & Kroll, S. (2020). Dynamics of toxigenic *Clostridium perfringens* colonisation in a cohort of prematurely born neonatal infants, *BMC Paediatrics*, 20, 75.
2. Odell, A., Eady, P. E., & **Dixon, R. A.** (2020). Spatio-temporal variability of AMR Enterobacteriaceae associated with a waste water effluent. *Environmental Pollution* (submitted).
3. Kay, S., Edwards, J., Brown, J., & **Dixon, R. A.** (2019). *Galleria mellonella* infection model identifies both high and low lethality of *Clostridium perfringens* toxigenic strains and their response to antimicrobials. *Frontiers in Microbiology,* 10, 1281.
4. Kiu, R., Brown, J., Bedwell, H., Leclaire, C., Caim, S., Pickard, D., Dougan, G., **Dixon, R. A,** & Hall. L/ (2019). Genomic analysis on broiler-associated *Clostridium perfringens* strains and exploratory caecal microbiome investigation reveals key factors linked to poultry necrotic enteritis. *Animal Microbiome*, 1(12), 1-14.

Participant Organisation 2	
Named staff members, details of specialism and expertise.	

Participant Organisation 3	
Named staff members, details of specialism and expertise.	

C. STAFF EFFORT

In the table below, please detail the staff time to be spent on the project (for every person named in section above) and their role in delivering the proposal If new staff will be hired in order to deliver the project please include their grade, name and the staff effort required.

Name and Role of Person where known/ Role of person to be recruited	Working hours per staff member on this project
Christian James (Principal Investigator), Senior Research Fellow; will oversee project, carry out much of the literature search (Tasks 1.1, 1.2, 1.3, 1.4), screening and collection of articles (Task 2.1), data extraction from articles (Task 3.1), writing of the final report (Tasks 4.1, 4.2), and dissemination.	259 h (35 days)
Luke Talbot (Co-Investigator), Research Assistant; will assist with the literature search (Tasks 1.1, 1.2, 1.3, 1.4), screening and collection of articles (Task 2.1), data extraction from articles (Task 3.1), and contribute to the writing of the final report (Task 4.1. 4.2), and dissemination.	407 h (55 days)
Stephen James (Co-Investigator), Director (Emeritus); will support the PI with the initial literature search (Tasks 1.1, 1.2, 1.3, 1.4) and screening of the literature collated in the initial literature search (Task 2.1), the data extraction from articles (Task 3.1), and contribute to the writing of the final report (Task 4.1. 4.2), and dissemination.	222 h (30 days)
Bukola Onarinde (Co-Investigator), Associate Professor; will be involved in agreeing the search criteria (Task 1.1), with the relevance screening of the literature collated in the initial literature search (Task 2.1), the data extraction from articles	187.5 h (25 days)

(Task 3.1), and contribute to the writing of the final report (Task 4.1. 4.2), and dissemination.	
Ronald Dixon (Co-Investigator), Reader; will be involved in agreeing the search criteria (Task 1.1), with the relevance screening of the literature collated in the initial literature search (Task 2.1), the data extraction from articles (Task 3.1), and contribute to the writing of the final report (Task 4.1. 4.2), and dissemination.	187.5 h (25 days)
Nicola Williams (External AMR consultant/expert), Professor; will act as an external AMR consultant/expert advisor to the project, particularly on aspects AMR aspects in a molecular context. Her expertise will be sought over the course of the project as and when molecular issues are of importance.	22.5 h (3 days)
Total staff effort	1285.5 h (173 days)

5: PROJECT MANAGEMENT
Please fully describe how the project will be managed to ensure that objectives and deliverables will be achieved on time and on budget. Please describe how different organisations/staff will interact to deliver the desired outcomes. Highlight any in-house or external accreditation for the project management system and how this relates to this project.
The project team responsible for designing and delivering the project are experienced and qualified in managing and implementing research, including running large and small multi-discipline, multi-partner Agency, DEFRA, Innovate UK, and EU projects. The project team will consist of the following members: **Christian James** (PI), **Luke Talbot**, **Stephen James**, **Bukola Onarinde** and **Ronald Dixon**. The PI will arrange monthly informal teleconference meetings (through MS Teams) with the project team to discuss progress, possible risks and ensure that the project is on target to deliver all of the objectives; at critical times (e.g. the start of the project) these may happen more frequently. Quarterly formal project meetings (again using MS Teams) will also be held, to which the Agency Project Officer will also be invited. In these meetings project progress and results will be formally reviewed and discussed. The meetings will provide a good opportunity for scientific discussions and making key decisions for the project. The project will also be subject to senior management scrutiny at the Grimsby Institute via regular project monitoring meetings that take place monthly to review project's progress and finances. Internally, at the Grimsby Institute, this project will be managed and controlled using Prince 2 principles. An internal Project Management Team will be established at the start of the project, comprising the three members of the FRPERC project team, plus the Executive Director of Projects and Partnerships (**Andy Goudie**), who will maintain oversight for the successful delivery of this project. His role will be to oversee the work programme and verify that all deliverables are on time and to the standard required. The team will meet on a regular basis (minimum monthly) to monitor and review budget, risk register, and performance against the delivery plan. In the event that the project diverts from the delivery plan, SMART targets will be designed, and recovery plans put in place, these will be monitored by the Executive Director for Projects and Partnerships. Project performance will be reported to the Institute's Senior Management Team and Corporation via the Executive Director, providing assurance that project activities will be scrutinised at the highest level. Regarding Risk Management, all relevant risks in delivering this project on time and to budget and how they will be managed by the project team are detailed in Section 6. The PI will create a risk register at the start of the project, which will be reviewed on a monthly basis, with the project team and at internal project monitoring meetings, to monitor the identified risks, to ensure any new risks which may impede the progress of the project are added to the register, and to ensure contingency plans are in place for such events. The project team meetings will primarily be monitoring and reviewing technical risks,

while the internal project monitoring meetings will be monitoring and reviewing risks in delivering the project on time and to budget.

Key personnel and their roles within this project are as follows:

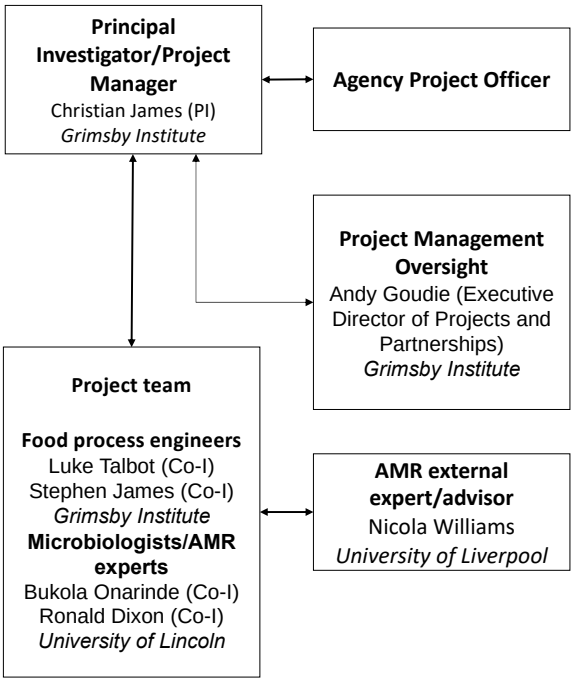
Christian James (FRPERC, Grimsby Institute) will act as the overall Principal Investigator and a consistent point of contact with the FSA Project Officer, reporting back to the Agency on a regular basis. He will be responsible for ensuring that the project proceeds according to the agreed plan, and formally agreeing any changes of the programme at each milestone decision point with the FSA Project Officer. He will also oversee and carry out much of the project design, literature search, screening process, collection of articles, review of articles, and writing of the final report. He will oversee the work programme, agree the detailed planning of the objectives and tasks and verify that all deliverables are on time and to the standard required.

Luke Talbot (FRPERC, Grimsby Institute), **Stephen James** (FRPERC, Grimsby Institute), **Bukola Onarinde** (University of Lincoln), and **Ronald Dixon** (University of Lincoln) will be Co-Investigators and will all be involved with the relevance screening of the literature collated in the initial literature search, data extraction and the critical review of the selected literature, and contribute to the writing of the final report (Task 2.2).

Nicola Williams (University of Liverpool) will act as an external AMR consultant/expert advisor to the project, particularly on aspects AMR aspects in a molecular context. Her expertise will be sought over the course of the project as and when molecular issues are of importance.

Andy Goudie (Grimsby Institute), Executive Director of Projects and Partnerships, will maintain oversight for the successful delivery of this project. He has led and supported the development of externally funded education, training and research projects for over 21 years. He has extensive experience in managing budgets and external relationships, achieving sector-leading project performance.

A diagram of how key personnel in this project will interact (organogram) is shown below:



6. RISK MANAGEMENT			
In the table provided, please identify all relevant risks in delivering this project on time and to budget. Briefly outline what steps will be taken to minimise these risks and how they will be managed by the project team. Please add more lines as required			
Identified risk	**Likelihood of risk (high, medium, low)**	**Impact of Risk (high, medium, low)**	**Risk management strategy**
Achieving Timeframe	Medium	Medium	Based upon significant past experience of similar projects, we have carefully considered the scope of the data collection and assessments required, and the time required to carry them out. Contingency has been built into the project plan for each Objective for delays in accessing or collating data. We have considered past challenges that have led to time overruns and built in a sensible catch-up phase for each objective. A full delivery plan and risk register will be implemented and maintained for this project, which will be overseen by an experienced project manager at Executive Director level. The project team will meet on a monthly basis to review progress to date. This will ensure that any variations from the delivery plan are identified, and remedial action is approved and directed in a timely manner.
Insufficient data available	Low	High	Lack of published data in the topic area of the impact of heat on AMR genes is beyond the control of the consortium. However, the well-structured and broad reaching paper search and evaluations processes detailed above will ensure that any relevant papers are collected. In the unlikely event that there is truly a dearth of basic information then by agreement with Agency at the mid-term review the project workplans will be modified to how best to address the gaps.
Too much data available	Medium	High	A preliminary search of articles has been conducted and suggests that this is a low risk. If excessive numbers of articles are revealed, a second pass with more specific keyword will be made to reduce to a manageable number of articles.
Data access challenges	Low	High	The Participant Organisations have access to the databases required for this work and access to the key academic journals that are likely to have relevant papers. Loss of access to paper abstracting services would have a major impact but this is highly unlikely as it is a central research tool used by the Participant Organisations. Contingency has been made in the budget for obtaining any paying for any additional

			access to papers / chapters / books / reports.
Data quality	Medium	High	In our previous Agency projects, carried out in the past 18 years, we have gathered extensive expertise in assessing and quantifying the quality of the data received. The data evaluation and screening procedures prescribed in the body of the work plan above will apply a weighting to reflect and accommodate the quality of data in each reviewed source.
Budget overruns	Low	Low	The budget has been compiled by an experienced team, who have carried out many projects of this nature over the past decades without overruns. We do not consider it a risk in this project. However, regular monitoring and tracking of expenditure will ensure potential budget over / underspend is identified and addressed at an early stage. This is a fixed price contract, so any budget overrun will be absorbed by the proposers, which mitigates all financial risk to the Agency.
A member of the project team falls ill or leaves	Low	Medium	Both Participant Organisations comprise a pool of experienced staff with directly relevant experience, sufficient to cover for sickness / if a staff member leaves. Whilst all project team members bring specific expertise to the work, the loss of one individual could be covered by the remaining members of the team. A team approach with several staff capable of covering most areas will significantly reduce impact if one person is unexpectedly unavailable for a short period of time.
Recruitment	Low	Low	Failure to recruit the required qualified staff is not a risk in this work, as the key specified staff are currently available to work on the proposed project. All the team will be in place and are available to work on this project from the 1st November 2020 onwards.
IP	Low	Low	The aim of the project is to review publicly available information. There are no expected IP issues.
Infrastructure: Loss of research facilities/resources due to emergency e.g. fire	Low	Low	Since the review will be desk-based work it should not be affected by any loss of specific host research facilities/resources. Back-up systems are in place and loss of access due to an IT network failures etc would only be temporary and not have a major impact in a 6-month project.
Disruption caused by current Coronavirus outbreak	Medium	High	We do not know at present whether the current shutdowns in place due to the Coronavirus outbreak will be still be in place when this project is due to start. If restrictions are still in place, they shouldn't

			impact on the project progress to much as the project is primarily desk based, the staff are used to working from home and distance working. Regular teleconferences will be used to maintain team working and cohesion.
Other Risks			The PI will create a risk register at the start of the project, which will be reviewed on a monthly basis to monitor identified risks, to ensure any new risks which may impede the progress of the project are added to the register, and to ensure contingency plans are in place for such events.

7. QUALITY MANAGEMENT

A. QUALITY MANAGEMENT

Please provide details of the measures that will be taken to manage and assure the quality of work. You should upload your Quality Assurance policy in the supporting documents section of your application.

This should include information on the quality assurance (QA) systems, , which have been implemented or are planned, and should be appropriate to the work concerned. All QA systems and procedures should be clear and auditable, and may include compliance with internationally accepted quality standards specified in the ITT e.g. ISO 9001 and ISO17025.

Specific to science projects and where relevant, applicants must indicate whether they would comply with the Joint Code of Practice for Research (JCoPR). If applicants do not already fully comply with the JCoPR please provide a statement to this effect to provide an explanation of how these requirements will be met. The FSA reserves the right to audit projects against the code and other quality standards

The lead principle investigator is responsible for all work carried out in the project; (including work supplied by sub-contractors) and should therefore ensure that the project is carried out in accordance with the Joint Code of Practice.

The Grimsby Institute and University of Lincoln are both aware of the requirements of the Joint Code of Practice for Research (JCoPR) and are committed to conducting research projects in accordance with good scientific practice. Having had wide experience of research projects all of the research teams and individuals involved in this project are aware of the need to ensure that all work is quality assured. This will be achieved through ensuring that Project goals and process are achieved in line with the proposed timeline; regular project progress reporting; regular supervision in relation to the Project with the supervisory team; feedback from participants within the Project. This project has been designed to comply with the joint code of practice for research.

Regarding the specific requirements of the Code, the lead PI shall endeavour to ensure that the project is carried out in accordance with the Code in the following ways:

QUALITY ISSUE	EVIDENCE
1. Responsibilities	An organisation structure showing line management responsibilities (organogram) for this project are shown in the proposal. We will consistently maintain and update a list of personnel involved with the project. We will have in place a documented agreement with our sub-contractor to adhere to JCoPR and evidence of rationale for appointment. We will maintain files documenting the roles & responsibilities for all project staff (including subcontractors) throughout the project.

2. Personnel competence	Brief CV's of all personnel associated with the project (including subcontractors) are contained within the proposal. Full CV's will be documented at the start of the project. We will maintain relevant, up-to-date training records for all project staff (including evidence showing awareness of obligation to comply with the Code's provisions).
3. Project planning	Since this is a desk-based project specific risk assessments are not required. Records will be maintained of the regular quarterly research project meetings that will include reviews of project timetables and plans. A proposed project plan with milestones and deliverables is contained in the proposal. This will be reviewed monthly by the lead organisation and quarterly by the research project team. Any changes will be formally agreed with the Agency. In a literature survey project of this nature we will decide on the most appropriate statistical method of scientifically quantifying the data when we know the amount and quality of the specifically relevant data. Any method will be agreed between the research project team and Agency. Documented, approved procedures for sampling materials is not required for this particular project. Ethical approval documentation and project licences are not required for this particular project.
4. Quality Control	Both Participant Organisations operate documented internal 'fit for purpose' review procedures Both Participant Organisations maintain records of consistently applied internal audits and any relevant findings and corrective actions to be taken will documented at quarterly project review meetings. Both Participant Organisations maintain an approved publication policy with authorisation procedures.
5. Health & safety	No specific documentation will be required for this particular desk-based project.
6. Handling of samples & materials	Not applicable to this particular desk-based project.
7. Facilities & equipment	A desk-based project of this nature only requires suitable computing, internet access, database access, and data storage facilities, which both Participant Organisations have. Collected data will be stored on secure independent back-up systems.
8. Documentation of procedures & methods	We maintain a robust process for document and version control in all key project documentation. Both Participant Organisations and research teams have carried out a number of similar literature survey projects of this nature and have therefore developed standard operating procedures for carrying out such work.
9.Research/work records	In this project the majority of the data will be collected and stored electronically, and the small amount of paper documentation collected will be scanned and held electronically. All raw data, searches and reports will be stored in a consistent file structure on a range of independent back-up systems. All data will be securely stored and regularly backed-up to secure systems. Both Participant Organisations have consistent and documented archiving procedures.
10. Field-based research	Not applicable to this particular project.

The Principal Investigator and Co-Investigators at Grimsby Institute and University of Lincoln have considerable experience in research and expertise in the managements of the projects of a similar

type, size, and timeframe. The project team, consisting of the following members: Christian James, Luke Talbot, Stephen James, Bukola Onarinde, and Ronald Dixon, will formally meet quarterly to discuss progress and make key decisions. In addition, regular informal meetings of the project team will take place to review the progress of the project against plan. The project will also be subject to senior management scrutiny at the Grimsby Institute via regular project monitoring meetings that take place monthly to review project's progress and finances.

FRPERC is part of the Grimsby institute, which has an institute-wide quality assurance policy covering externally funded research projects. FRPERC adheres to these policies and operates a fully documented task orientated job management structure. A fully audited set of records is produced for all studies or parts of studies undertaken by FRPERC. All research undertaken by FRPERC is subject to randomly selected internal audit and the research undertaken by the organisation as a whole is assessed by periodic external academic peer review. Standard operating procedures, protocols and risk assessments are prepared for all work. In addition, the Grimsby Institute conduct research for companies on a regular basis as well as for other publicity funded research bodies.

Researchers at the University of Lincoln operate within the Universities Code of Research Practice. The University of Lincoln conducts regular internal audits of projects.

B. ETHICS
Please identify the key ethical issues for this project and how these will be managed. Please respond to any issues raised in the Specification document Please describe the ethical issues of any involvement of people, human samples, animal research or personal data in this part. In addition, please describe the ethical review and governance arrangements that would apply to the work done. Applicants are reminded that, where appropriate, the need to obtain clearance for the proposed project from their local ethics committee. This is the responsibility of the project Lead Applicant. However, if a sub-contractor requires such clearance the project Lead Applicant should ensure that all relevant procedures have been followed. If there are no ethical issues please state this
There are no perceived ethical issues with this project.
C. DATA PROTECTION
Please identify any specific data protection issues for this project and how these will be managed. Please respond to any specific issues raised in the Specification document. Please note that the successful Applicant will be expected to comply with the Data Protection Act (DPA) 1998 and ensure that any information collected, processed and transferred on behalf of the FSA, will be held and transferred securely. In this part please provide details of the practices and systems which are in place for handling data securely including transmission between the field and head office and then to the FSA. Plans for how data will be deposited (i.e. within a community or institutional database/archive) and/or procedures for the destruction of physical and system data should also be included in this part (this is particularly relevant for survey data and personal data collected from clinical research trials). The project Lead Applicant will be responsible for ensuring that they and any sub-contractor who processes or handles information on behalf of the FSA are conducted securely.
We do not envisage any specific data protection issues with this project. Of course, any commercially sensitive information obtained from any participating stakeholders will remain confidential. Both teams at the Grimsby Institute and University of Lincoln will process any personal data provided to it in accordance with the EU General Data Protection Regulation (GDPR), which came in to force on the 25th May 2018, and any associated or subsequent legislation, Code of Practice or Statutory Instrument. Both institutions have established Data Protection Policies and procedures in accordance with current legislation. This policy applies to all staff, including temporary, casual or agency staff and contractors, consultants, research students, and suppliers working for, or on behalf of, either institution. They will take reasonable precautions to keep such personal data secure and to prevent unauthorised disclosure. Good research practice standards will be applied for the collection, management, and storage of all data collected.
D. SUSTAINABILITY

The Food Standards Agency is committed to improving sustainability in the management of operations. Procurement looks to its suppliers to help achieve this goal. You will need to demonstrate your approach to sustainability, in particular how you will apply it to this project taking into account economic, environmental and social aspects. This will be considered as part of our selection process and you must upload your organisations sustainability policies into the eligibility criteria in Bravo.
Please state what (if any) environmental certification you hold or briefly describe your current Environmental Management System (EMS)

The Grimsby Institute is committed to the systematic incorporation of environmental concern and social responsibility into their decisions and action. To indicate its commitment to its stakeholders the institution has adopted a number of key policies and strategies. The institution complies in all material respects with all applicable environmental laws and regulations in relations to their services. The institution has an Environmental Management System in place. The introduction of Environmental Management System (EMS) allows the institution to identify all Environmental Aspects associated with its operations and implement significant environmental improvements to reduce their impact on the environment. The Grimsby Institute has a five-year plan that has identified and prioritised actions to reduce its scope 1 & 2 CO_2 emissions by 10% by 2020/21 from 2015/16 levels saving £800k over the twenty-year lifetime of the installed technologies and reducing the carbon footprint of the estate by 205 tCO_2/annum.

The University of Lincoln is also committed to the systematic incorporation of environmental concern and social responsibility into their decisions and action. To indicate their commitment to their stakeholders, identify the key issues and act as a touchstone for their actions, the University has adopted a number of key policies and strategies. The University has a Sustainability Policy which is updated accordingly on an annual basis. The policy outlines the University's sustainability objectives and provides a clear commitment to comply with relevant legislation, regulations and other requirements. Progress against the policy is reviewed annually by the Sustainability Advisory Board. A detailed Sustainability Implementation Plan is in place which is owned and regularly updated by the Sustainability Officer. The plan is regularly reviewed at the Sustainability Advisory Board. The University is in the process of implementing BSACORN scheme, with the aim of becoming ISO. The introduction of an Environmental Management System (EMS) has allowed the University to identify all Environmental Aspects associated with its operations and implement significant environmental improvements to reduce the University's impact on the environment.

This project will make a use of email, audio, and video conference calls whenever possible to reduce travel and paper usage. The members of staff involved are currently employed in full time contracts. Expertise and knowledge generated will be kept in both institutions and be available for future projects and dissemination rather than be lost at the end of the project as may be the case with short term contracted project specific staff thus contributing to the sustainability of the UK food research community.

E. DISSEMINATION AND EXPLOITATION (Science Projects Only)

Where applicable please indicate how you intend to disseminate the results of this project, including written and verbal communication routes if appropriate. Applicants are advised to think carefully about how their research aligns with the FSA strategy, what is the impact that their research has on public health/ consumers and decide how the results can best be communicated to the relevant and appropriate people and organisations in as cost-effective manner as possible. Please provide as much detail as possible on what will be delivered. Any costs associated with this must be documented in the Financial Template.

The applicant should describe plans for the dissemination of the results for the project team as a whole and for individual participants. Details should include anticipated numbers of publications in refereed journals, articles in trade journals etc., presentations or demonstrations to the scientific community, trade organisations and internal reports or publications. Plans to make any information and/or reports available on the internet with the FSA's permission are also useful, however, this does not remove the requirement for Tenderers to think how best to target the output to relevant groups.
If a final report is part of the requirement, please make sure, as part of the executive summary, that aims and results are clear to the general audience and that the impact of the research on public health/consumers and it's alignment to FSA priorities is clearly stated.

Please note that permission to publish or to present findings from work supported by the FSA must be sought in advance from the relevant FSA Project Officer. The financial support of the FSA must also be acknowledged.

Please indicate whether any Intellectual Property (IP) may be generated by this project and how this could be exploited. Please be aware the FSA retains all rights to the intellectual property generated by any contract and where appropriate may exploit the IP generated for the benefit of public health. In this part Applicants should demonstrate the credibility of the partnership for exploitation of the results and explain the partnership's policy in respect of securing patents or granting licenses for the technology (if applicable). It should deal with any possible agreements between the partners to extend their co-operation in the exploitation phase and with relevant agreements with companies, in particular users, external to the partnership
We are aware of the Agency's commitment to openness and transparency. The expected output of this project will be a broad comprehensive critical review of the impact of heat treatment on AMR bacteria/genes, and a database of the publications included in the review, both suitable for publication on the FSA website. Following submission of the final report, the project team will discuss the key findings and recommendations arising from the research with the Agency. We also understand that the findings may also be required to be presented to ACMSF at a future meeting, and will be happy to do so. As well as the final project report being published by the Agency, we will agree with the Agency on appropriate methods to further disseminate the findings of this research to a wider audience. A full dissemination and exploitation plan will be agreed with the FSA Project Officer during the project. Example dissemination activities may include: • An executive summary document / press release agreed with the Agency and distributed to key stakeholders. • Placement of project summaries on the websites of FRPERC, Grimsby Institute and the Grimsby Institute Group, and the University of Lincoln which carry articles concerning R&D projects and a source of useful reference data for industry. • The ultimate findings are expected to be of scientific merit and at least one key paper will be submitted on "A comprehensive critical review of the impact of heat treatment on AMR bacteria/genes" for consideration for publication in a suitable peer-reviewed journal (such as Food Control or International Journal of Food Microbiology). • The presentation of results at any FSA conference, workshop, seminar or related event, as required. • Presenting, or supporting the presentation, of the findings of this work at a future FSA AMR 'show and tell' event, ACMSF (or AMR sub-group) meetings, and at a stakeholder meetings, if needed. • Assisting the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on any news story. The findings of this research will be disseminated bearing these points in mind: • The findings from throughout this project will be finalised and made public only after agreement of the FSA Project Officer has been obtained. • Any presentation of findings will include full acknowledgement of the funder (FSA) as providing financial support. The applicants have broad networks and contacts throughout the Agri-food industry that will be made available to support any dissemination activities, thus enabling widespread dissemination to a varied audience – industrial and academic.

Annex 4 – Supplier's Financial Proposal

Tender Reference	FS301059

Tender Title	Assessing the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria

Full legal organisation name	TEC Partnership (Grimsby Institute of Further & Higher Education)

[redacted]

Will you charge the Agency VAT on this proposal?	No

Please state your VAT registration number:	

Project Costs Summary Breakdown by Participating Organisations
Please include only the cost to the FSA.

[redacted]

Total Project Costs (excluding VAT) **	**£48,110.55**

* Please indicate zero, exempt or standard rate. VAT charges not identified above will not be paid by the FSA

** The total cost figure should be the same as the total cost shown in table 4
** The total cost figure should be the same as the total cost shown below and in the Schedule of payments tab.

Project Costs Summary

[redacted]

Total Project Costs	£48,110.55

[redacted]

Staff Costs Table

*This should reflect details entered in your technical application section 4C.
Please note that FSA is willing to accept pay rates based upon average pay costs. You will need to indicate where these have been used.

* Role or Position within the project	Participating Organisation	Daily Rate (£/Day)	* Daily Overhead Rate(£/Day)	Days to be spent on the project by all staff at this grade	**Total Cost (incl. overheads)**
[redacted]					
			Total Labour Costs		**£45,160.55**
			* Total Overhead Costs (if not shown above)		

Consumable/Equipment Costs

Please provide a breakdown of the consumables/equipment items you expect to consume during the project

Item	Quantity	Cost/Item(£)	Total
		£ -	£ -
	Total Material Costs		£ -

Please provide, in the table below, estimates of other costs that do not fit within any other cost headings

[redacted]		
		£ -
	Total Other Costs	£ 2,950.00

The Pricing Schedule

Proposed Project Start Date	01-Nov-2020	Amount				
Invoice Due Date	**Description as to which deliverables this invoice will refer to (*Please include the deliverable ref no(s) as appropriate*)**	***Net**	****** VAT Code**	**§ Duration from start of project (Weeks)**	**§ Duration from start of project (Date)**	**Financial Year**
	D1 & D2: Submit to FSA a summary of initial results					
[redacted]						
	relevant collated citations and abstracts (D2)					

	to the FSA					
	D3: Submit a mid-point					
[redacted]						
	and 3 to the FSA					
	D4: Submit					
[redacted]						
[redacted]						
	Total	**48,110.55**				

* Please insert the amount to be invoiced net of any VAT for each deliverable
** Please insert the applicable rate of VAT for each deliverable
*** 20% of the total project budget is withheld and will be paid upon acceptance of a satisfactory final report by the agency.
§The number of weeks after project commencement for the deliverable to be completed

Summary of Payments

Financial Year (Update as applicable in YYYY-YY format)	Year 1	Year 2		
	2020-21	2021-22	Retention	Total
Total Amount	[redacted]			**£48,110.55**

Short form Terms

1. Definitions used in the Contract

In this Contract, unless the context otherwise requires, the following words shall have the following meanings:

"Central Government Body"	means a body listed in one of the following sub-categories of the Central Government classification of the Public Sector Classification Guide, as published and amended from time to time by the Office for National Statistics: a) Government Department; b) Non-Departmental Public Body or Assembly Sponsored Public Body (advisory, executive, or tribunal); c) Non-Ministerial Department; or d) Executive Agency;
"Charges"	means the charges for the Deliverables as specified in the Order Form;
"Confidential Information"	means all information, whether written or oral (however recorded), provided by the disclosing Party to the receiving Party and which (i) is known by the receiving Party to be confidential; (ii) is marked as or stated to be confidential; or (iii) ought reasonably to be considered by the receiving Party to be confidential;
"Contract"	means the contract between (i) the Buyer and (ii) the Supplier which is created by the Supplier's counter signing the Order Form and includes the Order Form and Annexes;
"Controller"	has the meaning given to it in the GDPR;
"Buyer"	means the person identified in the letterhead of the Order Form;
"Date of Delivery"	means that date by which the Deliverables must be delivered to the Buyer, as specified in the Order Form;
"Buyer Cause"	any breach of the obligations of the Buyer or any other default, act, omission, negligence or statement of the Buyer, of its employees, servants, agents in connection with or in relation to the subject-matter of the Contract and in respect of which the Buyer is liable to the Supplier;

"Data Protection Legislation "	(i) the GDPR, the LED and any applicable national implementing Laws as amended from time to time (ii) the Data Protection Act 2018 to the extent that it relates to processing
	of personal data and privacy; (iii) all applicable Law about the processing of personal data and privacy;
"Data Protection Impact Assessment"	an assessment by the Controller of the impact of the envisaged processing on the protection of Personal Data;
"Data Protection Officer"	has the meaning given to it in the GDPR;
"Data Subject"	has the meaning given to it in the GDPR;
"Data Loss Event"	any event that results, or may result, in unauthorised access to Personal Data held by the Supplier under this Contract, and/or actual or potential loss and/or destruction of Personal Data in breach of this Contract, including any Personal Data Breach;
"Data Subject Access Request"	a request made by, or on behalf of, a Data Subject in accordance with rights granted pursuant to the Data Protection Legislation to access their Personal Data;
"Deliver"	means hand over the Deliverables to the Buyer at the address and on the date specified in the Order Form, which shall include unloading and any other specific arrangements agreed in accordance with Clause [ ]. Delivered and Delivery shall be construed accordingly;
"Existing IPR"	any and all intellectual property rights that are owned by or licensed to either Party and which have been developed independently of the Contract (whether prior to the date of the Contract or otherwise);
"Expiry Date"	means the date for expiry of the Contract as set out in the Order Form;
"FOIA"	means the Freedom of Information Act 2000 together with any guidance and/or codes of practice issued by the Information Commissioner or relevant Government department in relation to such legislation;

"Force Majeure Event"	any event, occurrence, circumstance, matter or cause affecting the performance by either Party of its obligations under the Contract arising from acts, events, omissions, happenings or non-happenings beyond its reasonable control which prevent or materially delay it from performing its obligations under the Contract but excluding: i) any industrial dispute relating to the Supplier, the Supplier Staff (including any subsets of them) or any other failure in the Supplier or the Subcontractor's supply chain; ii) any event, occurrence, circumstance, matter or cause which is attributable to the wilful act, neglect or failure to take reasonable precautions against it by the Party concerned; and iii) any failure of delay caused by a lack of funds;
"GDPR"	the General Data Protection Regulation (Regulation (EU) 2016/679);
"Goods"	means the goods to be supplied by the Supplier to the Buyer under the Contract;
"Good Industry Practice"	standards, practices, methods and procedures conforming to the law and the exercise of the degree of skill and care, diligence, prudence and foresight which would reasonably and ordinarily be expected from a skilled and experienced person or body engaged within the relevant industry or business sector;
"Government Data"	a) the data, text, drawings, diagrams, images or sounds (together with any database made up of any of these) which are embodied in any electronic, magnetic, optical or tangible media, including any of the Buyer's confidential information, and which: i) are supplied to the Supplier by or on behalf of the Buyer; or ii) the Supplier is required to generate, process, store or transmit pursuant to the Contract; or b) any Personal Data for which the Buyer is the Data Controller;
"Information"	has the meaning given under section 84 of the FOIA;
"Information Commissioner"	the UK's independent authority which deals with ensuring information relating to rights in the public interest and data privacy for individuals is met, whilst promoting openness by public bodies;

"Insolvency Event"	in respect of a person: a) if that person is insolvent; ii) if an order is made or a resolution is passed for the winding up of the person (other than voluntarily for the purpose of solvent amalgamation or reconstruction); iii) if an administrator or administrative receiver is appointed in respect of the whole or any part of the persons assets or business; iv) if the person makes any composition with its creditors or takes or suffers any similar or analogous action to any of the actions detailed in this definition as a result of debt in any jurisdiction;
"Key Personnel"	means any persons specified as such in the Order Form or otherwise notified as such by the Buyer to the Supplier in writing;
"LED"	Law Enforcement Directive (Directive (EU) 2016/680);
"New IPR"	all and intellectual property rights in any materials created or developed by or on behalf of the Supplier pursuant to the Contract but shall not include the Supplier's Existing IPR;
"Order Form"	means the letter from the Buyer to the Supplier printed above these terms and conditions;
"Party"	the Supplier or the Buyer (as appropriate) and "Parties" shall mean both of them;
"Personal Data"	has the meaning given to it in the GDPR;
"Personal Data Breach"	has the meaning given to it in the GDPR;
"Processor"	has the meaning given to it in the GDPR;
"Purchase Order Number"	means the Buyer's unique number relating to the order for Deliverables to be supplied by the Supplier to the Buyer in accordance with the terms of the Contract;
"Regulations"	the Public Contracts Regulations 2015 and/or the Public Contracts (Scotland) Regulations 2015 (as the context requires) as amended from time to time;
"Request for Information"	has the meaning set out in the FOIA or the Environmental Information Regulations 2004 as relevant (where the meaning set out for the term "request" shall apply);
"Services"	means the services to be supplied by the Supplier to the Buyer under the Contract;
"Specification"	means the specification for the Deliverables to be supplied by the Supplier to the Buyer (including as to quantity, description and quality) as specified in the Order Form;

"Staff"	means all directors, officers, employees, agents, consultants and contractors of the Supplier and/or of any sub-contractor of the Supplier engaged in the performance of the Supplier's obligations under the Contract;
"Staff Vetting Procedures"	means vetting procedures that accord with good industry practice or, where applicable, the Buyer's procedures for the vetting of personnel as provided to the Supplier from time to time;
"Subprocessor"	any third Party appointed to process Personal Data on behalf of the Supplier related to the Contract;
"Supplier Staff"	all directors, officers, employees, agents, consultants and contractors of the Supplier and/or of any Subcontractor engaged in the performance of the Supplier's obligations under a Contract;
"Supplier"	means the person named as Supplier in the Order Form;
"Term"	means the period from the start date of the Contract set out in the Order Form to the Expiry Date as such period may be extended in accordance with clause [ ] or terminated in accordance with the terms and conditions of the Contract;
"US-EU Privacy Shield Register"	a list of companies maintained by the United States of America Department for Commence that have self-certified their commitment to adhere to the European legislation relating to the processing of personal data to non-EU countries which is available online at: https://www.privacyshield.gov/list;
"VAT"	means value added tax in accordance with the provisions of the Value Added Tax Act 1994;
"Workers"	any one of the Supplier Staff which the Buyer, in its reasonable opinion, considers is an individual to which Procurement Policy Note 08/15 (Tax Arrangements of Public Appointees) (https://www.gov.uk/government/publications/procurement- policynote-0815-tax-arrangements-of-appointees) applies in respect of the Deliverables;
"Working Day"	means a day (other than a Saturday or Sunday) on which banks are open for business in the City of London.

2. Understanding the Contract

In the Contract, unless the context otherwise requires:

2.1 references to numbered clauses are references to the relevant clause in these terms and conditions;

2.2 any obligation on any Party not to do or omit to do anything shall include an obligation not to allow that thing to be done or omitted to be done;

2.3 the headings in this Contract are for information only and do not affect the interpretation of the Contract;

2.4 references to "writing" include printing, display on a screen and electronic transmission and other modes of representing or reproducing words in a visible form;

2.5 the singular includes the plural and vice versa;

2.6 a reference to any law includes a reference to that law as amended, extended, consolidated or re-enacted from time to time and to any legislation or byelaw made under that law; and

2.7 the word 'including', "for example" and similar words shall be understood as if they were immediately followed by the words "without limitation".

3. How the Contract works

3.1 The Order Form is an offer by the Buyer to purchase the Deliverables subject to and in accordance with the terms and conditions of the Contract.

3.2 The Supplier is deemed to accept the offer in the Order Form when the Buyer receives a copy of the Order Form signed by the Supplier.

3.3 The Supplier warrants and represents that its tender and all statements made and documents submitted as part of the procurement of Deliverables are and remain true and accurate.

4. What needs to be delivered

4.1 All Deliverables

(a) The Supplier must provide Deliverables: (i) in accordance with the Specification; (ii) to a professional standard; (iii) using reasonable skill and care; (iv) using Good Industry Practice; (v) using its own policies, processes and internal quality control measures as long as they don't conflict with the Contract; (vi) on the dates agreed; and (vii) that comply with all law.

(b) The Supplier must provide Deliverables with a warranty of at least 90 days (or longer where the Supplier offers a longer warranty period to its Buyers) from Delivery against all obvious defects.

4.2 Services clauses

(a) Late delivery of the Services will be a default of the Contract.

(b) The Supplier must co-operate with the Buyer and third party suppliers

on all aspects connected with the delivery of the Services and ensure that Supplier Staff comply with any reasonable instructions including any security requirements.

(c) The Buyer must provide the Supplier with reasonable access to its premises at reasonable times for the purpose of supplying the Services

(d) The Supplier must at its own risk and expense provide all equipment required to deliver the Services. Any equipment provided by the Buyer to the Supplier for supplying the Services remains the property of the Buyer and is to be returned to the Buyer on expiry or termination of the Contract.

(e) The Supplier must allocate sufficient resources and appropriate expertise to the Contract.

(f) The Supplier must take all reasonable care to ensure performance does not disrupt the Buyer's operations, employees or other contractors.

(g) On completion of the Services, the Supplier is responsible for leaving the Buyer's premises in a clean, safe and tidy condition and making good any damage that it has caused to the Buyer's premises or property, other than fair wear and tear.

(h) The Supplier must ensure all Services, and anything used to deliver the Services, are of good quality [and free from defects].

(i) The Buyer is entitled to withhold payment for partially or undelivered Services but doing so does not stop it from using its other rights under the Contract.

5. Pricing and payments

5.1 In exchange for the Deliverables, the Supplier shall be entitled to invoice the Buyer for the charges in the Order Form. The Supplier shall raise invoices promptly and in any event within 90 days from when the charges are due.

5.2 All Charges:

(a) exclude VAT, which is payable on provision of a valid VAT invoice;

(b) include all costs connected with the supply of Deliverables.

5.3 The Buyer must pay the Supplier the charges within 30 days of receipt by the Buyer of a valid, undisputed invoice, in cleared funds to the Supplier's account stated in the Order Form.

5.4 A Supplier invoice is only valid if it:

(a) includes all appropriate references including the Purchase Order Number and other details reasonably requested by the Buyer;

(b) includes a detailed breakdown of Deliverables which have been delivered (if any).

5.5 If there is a dispute between the Parties as to the amount invoiced, the Buyer shall pay the undisputed amount. The Supplier shall not suspend the provision of the Deliverables unless the Supplier is entitled to terminate the Contract for a failure to pay undisputed sums in accordance with clause 11.6. Any disputed amounts shall be resolved through the dispute resolution procedure detailed in clause 33.

5.6 The Buyer may retain or set-off payment of any amount owed to it by the Supplier if notice and reasons are provided.

5.7 The Supplier must ensure that all subcontractors are paid, in full, within 30 days of receipt of a valid, undisputed invoice. If this doesn't happen, the Buyer can publish the details of the late payment or non-payment.

6. The Buyer's obligations to the Supplier

6.1 If Supplier fails to comply with the Contract as a result of a Buyer Cause:
(a) the Buyer cannot terminate the Contract under clause 11;
(b) the Supplier is entitled to reasonable and proven additional expenses and to relief from liability under this Contract;
(c) the Supplier is entitled to additional time needed to deliver the Deliverables;
(d) the Supplier cannot suspend the ongoing supply of Deliverables.

6.2 Clause 6.1 only applies if the Supplier:
(a) gives notice to the Buyer within 10 Working Days of becoming aware;
(b) demonstrates that the failure only happened because of the Buyer Cause;
(c) mitigated the impact of the Buyer Cause.

7. Record keeping and reporting

7.1 The Supplier must ensure that suitably qualified representatives attend progress meetings with the Buyer and provide progress reports when specified in the Order Form.

7.2 The Supplier must keep and maintain full and accurate records and accounts on everything to do with the Contract for seven years after the date of expiry or termination of the Contract.

7.3 The Supplier must allow any auditor appointed by the Buyer access to their premises to verify all contract accounts and records of everything to do with the Contract and provide copies for the audit.

7.4 The Supplier must provide information to the auditor and reasonable co-operation at their request.

7.5 If the Supplier is not providing any of the Deliverables, or is unable to provide

them, it must immediately:
(a) tell the Buyer and give reasons;
(b) propose corrective action;
(c) provide a deadline for completing the corrective action.

7.6 If the Buyer, acting reasonably, is concerned as to the financial stability of the Supplier such that it may impact on the continued performance of the Contract then the Buyer may:
(a) require that the Supplier provide to the Buyer (for its approval) a plan setting out how the Supplier will ensure continued performance of the Contract and the Supplier will make changes to such plan as reasonably required by the Buyer and once it is agreed then the Supplier shall act in accordance with such plan and report to the Buyer on demand
(b) if the Supplier fails to provide a plan or fails to agree any changes which are requested by the Buyer or fails to implement or provide updates on progress with the plan, terminate the Contract immediately for material breach (or on such date as the Buyer notifies).

8. Supplier staff

8.1 The Supplier Staff involved in the performance of the Contract must:
(a) be appropriately trained and qualified;
(b) be vetted using Good Industry Practice;
(c) comply with all conduct requirements when on the Buyer's premises.

8.2 Where a Buyer decides one of the Supplier's Staff isn't suitable to work on the Contract, the Supplier must replace them with a suitably qualified alternative.

8.3 If requested, the Supplier must replace any person whose acts or omissions have caused the Supplier to breach clause 8.

8.4 The Supplier must provide a list of Supplier Staff needing to access the Buyer's premises and say why access is required.

8.5 The Supplier indemnifies the Buyer against all claims brought by any person employed by the Supplier caused by an act or omission of the Supplier or any Supplier Staff.

8.6 The Supplier shall use those persons nominated in the Order Form (if any) to provide the Deliverables and shall not remove or replace any of them unless:
(a) requested to do so by the Buyer (not to be unreasonably withheld or delayed);
(b) the person concerned resigns, retires or dies or is on maternity or long-term sick leave; or
(c) the person's employment or contractual arrangement with the Supplier or any subcontractor is terminated for material breach of contract by the employee.

9. Rights and protection

9.1 The Supplier warrants and represents that:

(a) it has full capacity and authority to enter into and to perform the Contract;

(b) the Contract is executed by its authorised representative;

(c) it is a legally valid and existing organisation incorporated in the place it was formed;

(d) there are no known legal or regulatory actions or investigations before any court, administrative body or arbitration tribunal pending or threatened against it or its affiliates that might affect its ability to perform the Contract;

(e) it maintains all necessary rights, authorisations, licences and consents to perform its obligations under the Contract;

(f) it doesn't have any contractual obligations which are likely to have a material adverse effect on its ability to perform the Contract; and

(g) it is not impacted by an Insolvency Event.

9.2 The warranties and representations in clause 9.1 are repeated each time the Supplier provides Deliverables under the Contract.

9.3 The Supplier indemnifies the Buyer against each of the following:

(a) wilful misconduct of the Supplier, any of its subcontractor and/or Supplier Staff that impacts the Contract;

(b) non-payment by the Supplier of any tax or National Insurance.

9.4 If the Supplier becomes aware of a representation or warranty that becomes untrue or misleading, it must immediately notify the Buyer.

9.5 All third party warranties and indemnities covering the Deliverables must be assigned for the Buyer's benefit by the Supplier.

10. Intellectual Property Rights (IPRs)

10.1 Each Party keeps ownership of its own Existing IPRs. The Supplier gives the Buyer a non-exclusive, perpetual, royalty-free, irrevocable, transferable worldwide licence to use, change and sub-license the Supplier's Existing IPR to enable it and its sub- licensees to both:

(a) receive and use the Deliverables;

(b) use the New IPR.

10.2 Any New IPR created under the Contract is owned by the Buyer. The Buyer gives the Supplier a licence to use any Existing IPRs for the purpose of fulfilling its obligations under the Contract and a perpetual, royalty-free, non-exclusive licence to use any New IPRs.

10.3 Where a Party acquires ownership of intellectual property rights incorrectly under this Contract it must do everything reasonably necessary to complete a transfer assigning them in writing to the other Party on request and at its own cost.

10.4 Neither Party has the right to use the other Party's intellectual property rights, including any use of the other Party's names, logos or trademarks, except as provided in clause 10 or otherwise agreed in writing.

10.5 If any claim is made against the Buyer for actual or alleged infringement of a third party's intellectual property arising out of, or in connection with, the supply or use of the Deliverables (an "**IPR Claim**"), then the Supplier indemnifies the Buyer against all losses, damages, costs or expenses (including professional fees and fines) incurred as a result of the IPR Claim.

10.6 If an IPR Claim is made or anticipated the Supplier must at its own expense and the Buyer's sole option, either:

(a) obtain for the Buyer the rights in clauses 10.1 and 10.2 without infringing any third party intellectual property rights;

(b) replace or modify the relevant item with substitutes that don't infringe intellectual property rights without adversely affecting the functionality or performance of the Deliverables.

11. Ending the contract

11.1 The Contract takes effect on the date of or (if different) the date specified in the Order Form and ends on the earlier of the date of expiry or termination of the Contract or earlier if required by Law.

11.2 The Buyer can extend the Contract where set out in the Order Form in accordance with the terms in the Order Form.

11.3 Ending the Contract without a reason

The Buyer has the right to terminate the Contract at any time without reason or liability by giving the Supplier not less than 90 days' written notice and if it's terminated clause 11.5(b) to 11.5(g) applies.

11.4 When the Buyer can end the Contract

(a) If any of the following events happen, the Buyer has the right to immediately terminate its Contract by issuing a termination notice in writing to the Supplier:

(i) there's a Supplier Insolvency Event;

(ii) if the Supplier repeatedly breaches the Contract in a way to reasonably justify the opinion that its conduct is inconsistent with it having the intention or ability to give effect to the terms and conditions of the Contract;

(iii) if the Supplier is in material breach of any obligation which is capable of remedy, and that breach is not remedied within 30 days of the Supplier receiving notice specifying the breach and requiring it to be remedied;

(iv) there's a change of control (within the meaning of section 450 of the Corporation Tax Act 2010) of the Supplier which isn't pre-approved by the Buyer in writing;

(v) if the Buyer discovers that the Supplier was in one of the situations in 57 (1) or 57(2) of the Regulations at the time the Contract was awarded;

(vi) the Court of Justice of the European Union uses Article 258 of the Treaty on the Functioning of the European Union (TFEU) to declare that the Contract should not have been awarded to the Supplier because of a serious breach of the TFEU or the Regulations;

(vii) the Supplier or its affiliates embarrass or bring the Buyer into disrepute or diminish the public trust in them.

(b) If any of the events in 73(1) (a) to (c) of the Regulations (substantial modification, exclusion of the Supplier, procurement infringement) happen, the Buyer has the right to immediately terminate the Contract and clause 11.5(b) to 11.5(g) applies.

11.5 What happens if the Contract ends

Where the Buyer terminates the Contract under clause 11.4(a) all of the following apply:

(a) the Supplier is responsible for the Buyer's reasonable costs of procuring replacement deliverables for the rest of the term of the Contract;

(b) the Buyer's payment obligations under the terminated Contract stop immediately;

(c) accumulated rights of the Parties are not affected;

(d) the Supplier must promptly delete or return the Government Data except where required to retain copies by law;

(e) the Supplier must promptly return any of the Buyer's property provided under the Contract;

(f) the Supplier must, at no cost to the Buyer, give all reasonable assistance to the Buyer and any incoming supplier and co-operate fully in the handover and re-procurement;

(g) the following clauses survive the termination of the Contract: [3.2.10, 6, 7.2, 9, 11, 14, 15, 16, 17, 18, 34, 35] and any clauses which are expressly or by implication intended to continue.

11.6 When the Supplier can end the Contract

(a) The Supplier can issue a reminder notice if the Buyer does not pay an undisputed invoice on time. The Supplier can terminate the Contract if the Buyer fails to pay an undisputed invoiced sum due and worth over 10% of the total Contract value or £1,000, whichever is the lower, within 30 days of the date of the reminder notice.

(b) If a Supplier terminates the Contract under clause 11.6(a):

(i) the Buyer must promptly pay all outstanding charges incurred to the Supplier;

(ii) the Buyer must pay the Supplier reasonable committed and unavoidable losses as long as the Supplier provides a fully itemised and costed schedule with evidence - the maximum value of this payment is limited to the total sum payable to the Supplier

if the Contract had not been terminated;

(iii) clauses 11.5(d) to 11.5(g) apply.

11.7 Partially ending and suspending the Contract

(a) Where the Buyer has the right to terminate the Contract it can terminate or suspend (for any period), all or part of it. If the Buyer suspends the Contract it can provide the Deliverables itself or buy them from a third party.

(b) The Buyer can only partially terminate or suspend the Contract if the remaining parts of it can still be used to effectively deliver the intended purpose.

(c) The Parties must agree (in accordance with clause 24) any necessary variation required by clause 11.7, but the Supplier may not either:

(i) reject the variation;

(ii) increase the Charges, except where the right to partial termination is under clause 11.3.

(d) The Buyer can still use other rights available, or subsequently available to it if it acts on its rights under clause 11.7.

12. How much you can be held responsible for

12.1 Each Party's total aggregate liability under or in connection with the Contract (whether in tort, contract or otherwise) is no more than 125% of the Charges paid or payable to the Supplier.

12.2 No Party is liable to the other for:

(a) any indirect losses;

(b) loss of profits, turnover, savings, business opportunities or damage to goodwill (in each case whether direct or indirect).

12.3 In spite of clause 12.1, neither Party limits or excludes any of the following:

(a) its liability for death or personal injury caused by its negligence, or that of its employees, agents or subcontractors;

(b) its liability for bribery or fraud or fraudulent misrepresentation by it or its employees;

(c) any liability that cannot be excluded or limited by law.

12.4 In spite of clause 12.1, the Supplier does not limit or exclude its liability for any indemnity given under clauses 4.2(j), 4.2(m), 8.5, 9.3, 10.5, 13.2, 14.26(e) or 30.2(b).

12.5 Each Party must use all reasonable endeavours to mitigate any loss or damage which it suffers under or in connection with the Contract, including any indemnities.

12.6 If more than one Supplier is party to the Contract, each Supplier Party is fully responsible for both their own liabilities and the liabilities of the other Suppliers.

13. Obeying the law

13.1 The Supplier must, in connection with provision of the Deliverables, use reasonable endeavours to:

(a) comply and procure that its subcontractors comply with the Supplier Code of Conduct appearing at (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/a ttachment_data/file/779660/20190220-Supplier_Code_of_Conduct.pdf) and such other corporate social responsibility requirements as the Buyer may notify to the Supplier from time to time;

(b) support the Buyer in fulfilling its Public Sector Equality duty under S149 of the Equality Act 2010;

(c) not use nor allow its subcontractors to use modern slavery, child labour or inhumane treatment;

(d) meet the applicable Government Buying Standards applicable to Deliverables which can be found online at: https://www.gov.uk/government/collections/sustainable-procurement-the- government-buying-standards-gbs

13.2 The Supplier indemnifies the Buyer against any costs resulting from any default by the Supplier relating to any applicable law to do with the Contract.

13.3 The Supplier must appoint a Compliance Officer who must be responsible for ensuring that the Supplier complies with Law, Clause 13.1 and Clauses 27 to 32

13.4 "Compliance Officer" the person(s) appointed by the Supplier who is responsible for ensuring that the Supplier complies with its legal obligations;

14. Data protection

14.1 The Buyer is the Controller and the Supplier is the Processor for the purposes of the Data Protection Legislation.

14.2 The Supplier must process Personal Data and ensure that Supplier Staff process Personal Data only in accordance with this Contract.

14.3 The Supplier must not remove any ownership or security notices in or relating to the Government Data.

14.4 The Supplier must make accessible back-ups of all Government Data, stored in an agreed off-site location and send the Buyer copies every six Months.

14.5 The Supplier must ensure that any Supplier system holding any Government Data, including back-up data, is a secure system that complies with the security requirements specified [in writing] by the Buyer.

14.6 If at any time the Supplier suspects or has reason to believe that the Government Data provided under the Contract is corrupted, lost or sufficiently degraded, then the Supplier must notify the Buyer and immediately suggest remedial action.

14.7 If the Government Data is corrupted, lost or sufficiently degraded so as to be unusable the Buyer may either or both:
(a) tell the Supplier to restore or get restored Government Data as soon as practical but no later than five Working Days from the date that the Buyer receives notice, or the Supplier finds out about the issue, whichever is earlier;
(b) restore the Government Data itself or using a third party.

14.8 The Supplier must pay each Party's reasonable costs of complying with clause 14.7 unless the Buyer is at fault.

14.9 Only the Buyer can decide what processing of Personal Data a Supplier can do under the Contract and must specify it for the Contract using the template in Annex 1 of the Order Form (*Authorised Processing*).

14.10 The Supplier must only process Personal Data if authorised to do so in the Annex to the Order Form (*Authorised Processing*) by the Buyer. Any further written instructions relating to the processing of Personal Data are incorporated into Annex 1 of the Order Form.

14.11 The Supplier must give all reasonable assistance to the Buyer in the preparation of any Data Protection Impact Assessment before starting any processing, including:
(a) a systematic description of the expected processing and its purpose;
(b) the necessity and proportionality of the processing operations;
(c) the risks to the rights and freedoms of Data Subjects;
(d) the intended measures to address the risks, including safeguards, security measures and mechanisms to protect Personal Data.

14.12 The Supplier must notify the Buyer immediately if it thinks the Buyer's instructions breach the Data Protection Legislation.

14.13 The Supplier must put in place appropriate Protective Measures to protect against a Data Loss Event which must be approved by the Buyer.

14.14 If lawful to notify the Buyer, the Supplier must notify it if the Supplier is required to process Personal Data by Law promptly and before processing it.

14.15 The Supplier must take all reasonable steps to ensure the reliability and integrity of any Supplier Staff who have access to the Personal Data and ensure that they:
(a) are aware of and comply with the Supplier's duties under this clause 11;
(b) are subject to appropriate confidentiality undertakings with the Supplier

or any Subprocessor;

(c) are informed of the confidential nature of the Personal Data and do not provide any of the Personal Data to any third Party unless directed in writing to do so by the Buyer or as otherwise allowed by the Contract;

(d) have undergone adequate training in the use, care, protection and handling of Personal Data.

14.16 The Supplier must not transfer Personal Data outside of the EU unless all of the following are true:

(a) it has obtained prior written consent of the Buyer;

(b) the Buyer has decided that there are appropriate safeguards (in accordance with Article 46 of the GDPR);

(c) the Data Subject has enforceable rights and effective legal remedies when transferred;

(d) the Supplier meets its obligations under the Data Protection Legislation by providing an adequate level of protection to any Personal Data that is transferred;

(e) where the Supplier is not bound by Data Protection Legislation it must use its best endeavours to help the Buyer meet its own obligations under Data Protection Legislation; and

(f) the Supplier complies with the Buyer's reasonable prior instructions about the processing of the Personal Data.

14.17 The Supplier must notify the Buyer immediately if it:

(a) receives a Data Subject Access Request (or purported Data Subject Access Request);

(b) receives a request to rectify, block or erase any Personal Data;

(c) receives any other request, complaint or communication relating to either Party's obligations under the Data Protection Legislation;

(d) receives any communication from the Information Commissioner or any other regulatory authority in connection with Personal Data processed under this Contract;

(e) receives a request from any third Party for disclosure of Personal Data where compliance with the request is required or claims to be required by Law;

(f) becomes aware of a Data Loss Event.

14.18 Any requirement to notify under clause 14.17 includes the provision of further information to the Buyer in stages as details become available.

14.19 The Supplier must promptly provide the Buyer with full assistance in relation to any Party's obligations under Data Protection Legislation and any complaint, communication or request made under clause 14.17. This includes giving the Buyer:

(a) full details and copies of the complaint, communication or request;

(b) reasonably requested assistance so that it can comply with a Data Subject Access Request within the relevant timescales in the Data Protection Legislation;

(c) any Personal Data it holds in relation to a Data Subject on request;

(d) assistance that it requests following any Data Loss Event;

(e) assistance that it requests relating to a consultation with, or request from, the Information Commissioner's Office.

14.20 The Supplier must maintain full, accurate records and information to show it complies with this clause 14. This requirement does not apply where the Supplier employs fewer than 250 staff, unless either the Buyer determines that the processing:
(a) is not occasional;
(b) includes special categories of data as referred to in Article 9(1) of the GDPR or Personal Data relating to criminal convictions and offences referred to in Article 10 of the GDPR;
(c) is likely to result in a risk to the rights and freedoms of Data Subjects.

14.21 The Supplier must appoint a Data Protection Officer responsible for observing its obligations in this Schedule and give the Buyer their contact details.

14.22 Before allowing any Subprocessor to process any Personal Data, the Supplier must:
(a) notify the Buyer in writing of the intended Subprocessor and processing;
(b) obtain the written consent of the Buyer;
(c) enter into a written contract with the Subprocessor so that this clause 14 applies to the Subprocessor;
(d) provide the Buyer with any information about the Subprocessor that the Buyer reasonably requires.

14.23 The Supplier remains fully liable for all acts or omissions of any Subprocessor.

14.24 At any time the Buyer can, with 30 Working Days notice to the Supplier, change this clause 14 to:
(a) replace it with any applicable standard clauses (between the controller and processor) or similar terms forming part of an applicable certification scheme under GDPR Article 42;
(b) ensure it complies with guidance issued by the Information Commissioner's Office.

14.25 The Parties agree to take account of any non-mandatory guidance issued by the Information Commissioner's Office.

14.26 The Supplier:
(a) must provide the Buyer with all Government Data in an agreed open format within 10 Working Days of a written request;
(b) must have documented processes to guarantee prompt availability of Government Data if the Supplier stops trading;
(c) must securely destroy all Storage Media that has held Government Data at the end of life of that media using Good Industry Practice;
(d) securely erase all Government Data and any copies it holds when asked to do so by the Buyer unless required by Law to retain it;
(e) indemnifies the Buyer against any and all Losses incurred if the Supplier breaches clause 14 and any Data Protection Legislation.

15. What you must keep confidential

15.1 Each Party must:
- (a) keep all Confidential Information it receives confidential and secure;
- (b) not disclose, use or exploit the disclosing Party's Confidential Information without the disclosing Party's prior written consent, except for the purposes anticipated under the Contract;
- (c) immediately notify the disclosing Party if it suspects unauthorised access, copying, use or disclosure of the Confidential Information.

15.2 In spite of clause 15.1, a Party may disclose Confidential Information which it receives from the disclosing Party in any of the following instances:
- (a) where disclosure is required by applicable Law or by a court with the relevant jurisdiction if the recipient Party notifies the disclosing Party of the full circumstances, the affected Confidential Information and extent of the disclosure;
- (b) if the recipient Party already had the information without obligation of confidentiality before it was disclosed by the disclosing Party;
- (c) if the information was given to it by a third party without obligation of confidentiality;
- (d) if the information was in the public domain at the time of the disclosure;
- (e) if the information was independently developed without access to the disclosing Party's Confidential Information;
- (f) to its auditors or for the purposes of regulatory requirements;
- (g) on a confidential basis, to its professional advisers on a need-to-know basis;
- (h) to the Serious Fraud Office where the recipient Party has reasonable grounds to believe that the disclosing Party is involved in activity that may be a criminal offence under the Bribery Act 2010.

15.3 The Supplier may disclose Confidential Information on a confidential basis to Supplier Staff on a need-to-know basis to allow the Supplier to meet its obligations under the Contract. The Supplier Staff must enter into a direct confidentiality agreement with the Buyer at its request.

15.4 The Buyer may disclose Confidential Information in any of the following cases:
- (a) on a confidential basis to the employees, agents, consultants and contractors of the Buyer;
- (b) on a confidential basis to any other Central Government Body, any successor body to a Central Government Body or any company that the Buyer transfers or proposes to transfer all or any part of its business to;
- (c) if the Buyer (acting reasonably) considers disclosure necessary or appropriate to carry out its public functions;

(d) where requested by Parliament;
(e) under clauses 5.7 and 16.

15.5 For the purposes of clauses 15.2 to 15.4 references to disclosure on a confidential basis means disclosure under a confidentiality agreement or arrangement including terms as strict as those required in clause 15.

15.6 Information which is exempt from disclosure by clause 16 is not Confidential Information.

15.7 The Supplier must not make any press announcement or publicise the Contract or any part of it in any way, without the prior written consent of the Buyer and must take all reasonable steps to ensure that Supplier Staff do not either.

16. When you can share information

16.1 The Supplier must tell the Buyer within 48 hours if it receives a Request For Information.

16.2 Within the required timescales the Supplier must give the Buyer full co-operation and information needed so the Buyer can:
(a) comply with any Freedom of Information Act (FOIA) request;
(b) comply with any Environmental Information Regulations (EIR) request.

16.3 The Buyer may talk to the Supplier to help it decide whether to publish information under clause 16. However, the extent, content and format of the disclosure is the Buyer's decision, which does not need to be reasonable.

17. Invalid parts of the contract

If any part of the Contract is prohibited by Law or judged by a court to be unlawful, void or unenforceable, it must be read as if it was removed from that Contract as much as required and rendered ineffective as far as possible without affecting the rest of the Contract, whether it's valid or enforceable.

18. No other terms apply

The provisions incorporated into the Contract are the entire agreement between the Parties. The Contract replaces all previous statements and agreements whether written or oral. No other provisions apply.

19. Other people's rights in a contract

No third parties may use the Contracts (Rights of Third Parties) Act (CRTPA) to enforce any term of the Contract unless stated (referring to CRTPA) in the Contract. This does not affect

third party rights and remedies that exist independently from CRTPA.

20. Circumstances beyond your control

20.1 Any Party affected by a Force Majeure Event is excused from performing its obligations under the Contract while the inability to perform continues, if it both:

(a) provides written notice to the other Party;
(b) uses all reasonable measures practical to reduce the impact of the Force Majeure Event.

20.2 Either party can partially or fully terminate the Contract if the provision of the Deliverables is materially affected by a Force Majeure Event which lasts for 90 days continuously.

20.3 Where a Party terminates under clause 20.2:
(a) each party must cover its own losses;
(b) clause 11.5(b) to 11.5(g) applies.

21. Relationships created by the contract

The Contract does not create a partnership, joint venture or employment relationship. The Supplier must represent themselves accordingly and ensure others do so.

22. Giving up contract rights

A partial or full waiver or relaxation of the terms of the Contract is only valid if it is stated to be a waiver in writing to the other Party.

23. Transferring responsibilities

23.1 The Supplier cannot assign the Contract without the Buyer's written consent.

23.2 The Buyer can assign, novate or transfer its Contract or any part of it to any Crown Body, public or private sector body which performs the functions of the Buyer.

23.3 When the Buyer uses its rights under clause 23.2 the Supplier must enter into a novation agreement in the form that the Buyer specifies.

23.4 The Supplier can terminate the Contract novated under clause 23.2 to a private sector body that is experiencing an Insolvency Event.

23.5 The Supplier remains responsible for all acts and omissions of the Supplier Staff as if they were its own.

23.6 If the Buyer asks the Supplier for details about Subcontractors, the Supplier must provide details of Subcontractors at all levels of the supply chain including:
(a) their name;
(b) the scope of their appointment;
(c) the duration of their appointment.

24. Changing the contract

24.1 Either Party can request a variation to the Contract which is only effective if agreed in writing and signed by both Parties. The Buyer is not required to accept a variation request made by the Supplier.

25. How to communicate about the contract

25.1 All notices under the Contract must be in writing and are considered effective on the Working Day of delivery as long as they're delivered before 5:00pm on a Working Day. Otherwise the notice is effective on the next Working Day. An email is effective when sent unless an error message is received.

25.2 Notices to the Buyer or Supplier must be sent to their address in the Order Form.

25.3 This clause does not apply to the service of legal proceedings or any documents in any legal action, arbitration or dispute resolution.

26. Preventing fraud, bribery and corruption

26.1 The Supplier shall not:

(a) commit any criminal offence referred to in the Regulations 57(1) and 57(2);

(b) offer, give, or agree to give anything, to any person (whether working for or engaged by the Buyer or any other public body) an inducement or reward for doing, refraining from doing, or for having done or refrained from doing, any act in relation to the obtaining or execution of the Contract or any other public function or for showing or refraining from showing favour or disfavour to any person in relation to the Contract or any other public function.

26.2 The Supplier shall take all reasonable steps (including creating, maintaining and enforcing adequate policies, procedures and records), in accordance with good industry practice, to prevent any matters referred to in clause 26.1 and any fraud by the Staff and the Supplier (including its shareholders, members and directors) in connection with the Contract and shall notify the Buyer immediately if it has reason to suspect that any such matters have occurred or is occurring or is likely to occur.

26.3 If the Supplier or the Staff engages in conduct prohibited by clause 26.1 or commits fraud in relation to the Contract or any other contract with the Crown (including the Buyer) the Buyer may:

(a) terminate the Contract and recover from the Supplier the amount of any loss suffered by the Buyer resulting from the termination, including the cost reasonably incurred by the Buyer of making other arrangements for the supply of the Deliverables and any additional expenditure incurred by the Buyer throughout the remainder of the Contract; or

(b) recover in full from the Supplier any other loss sustained by the Buyer in consequence of any breach of this clause.

27. Equality, diversity and human rights

27.1 The Supplier must follow all applicable equality law when they perform their obligations under the Contract, including:

(a) protections against discrimination on the grounds of race, sex, gender reassignment, religion or belief, disability, sexual orientation, pregnancy, maternity, age or otherwise;

(b) any other requirements and instructions which the Buyer reasonably imposes related to equality Law.

27.2 The Supplier must take all necessary steps, and inform the Buyer of the steps taken, to prevent anything that is considered to be unlawful discrimination by any court or tribunal, or the Equality and Human Rights Commission (or any successor organisation) when working on the Contract.

28. Health and safety

28.1 The Supplier must perform its obligations meeting the requirements of:

(a) all applicable law regarding health and safety;

(b) the Buyer's current health and safety policy while at the Buyer's premises, as provided to the Supplier.

28.2 The Supplier and the Buyer must as soon as possible notify the other of any health and safety incidents or material hazards they're aware of at the Buyer premises that relate to the performance of the Contract.

29. Environment

29.1 When working on Site the Supplier must perform its obligations under the Buyer's current Environmental Policy, which the Buyer must provide.

29.2 The Supplier must ensure that Supplier Staff are aware of the Buyer's Environmental Policy.

30. Tax

30.1 The Supplier must not breach any tax or social security obligations and must enter into a binding agreement to pay any late contributions due, including where applicable, any interest or any fines. The Buyer cannot terminate the Contract where the Supplier has not paid a minor tax or social security contribution.

30.2 Where the Supplier or any Supplier Staff are liable to be taxed or to pay National Insurance contributions in the UK relating to payment received under the Off Contract, the Supplier must both:

(a) comply with the Income Tax (Earnings and Pensions) Act 2003 and all other statutes and regulations relating to income tax, the Social Security Contributions and Benefits Act 1992 (including IR35) and National Insurance contributions;

(b) indemnify the Buyer against any Income Tax, National Insurance and social security contributions and any other liability, deduction, contribution, assessment or claim arising from or made during or after the Contract Period in connection with the provision

of the Deliverables by the Supplier or any of the Supplier Staff.

30.3 If any of the Supplier Staff are Workers who receive payment relating to the Deliverables, then the Supplier must ensure that its contract with the Worker contains the following requirements:

(a) the Buyer may, at any time during the term of the Contract, request that the Worker provides information which demonstrates they comply with clause 30.2, or why those requirements do not apply, the Buyer can specify the information the Worker must provide and the deadline for responding;

(b) the Worker's contract may be terminated at the Buyer's request if the Worker fails to provide the information requested by the Buyer within the time specified by the Buyer;

(c) the Worker's contract may be terminated at the Buyer's request if the Worker provides information which the Buyer considers isn't good enough to demonstrate how it complies with clause 30.2 or confirms that the Worker is not complying with those requirements;

(d) the Buyer may supply any information they receive from the Worker to HMRC for revenue collection and management.

31. Conflict of interest

31.1 The Supplier must take action to ensure that neither the Supplier nor the Supplier Staff are placed in the position of an actual or potential conflict between the financial or personal duties of the Supplier or the Supplier Staff and the duties owed to the Buyer under the Contract, in the reasonable opinion of the Buyer.

31.2 The Supplier must promptly notify and provide details to the Buyer if a conflict of interest happens or is expected to happen.

31.3 The Buyer can terminate its Contract immediately by giving notice in writing to the Supplier or take any steps it thinks are necessary where there is or may be an actual or potential conflict of interest.

32. Reporting a breach of the contract

32.1 As soon as it is aware of it the Supplier and Supplier Staff must report to the Buyer any actual or suspected breach of law, clause 13.1, or clauses 26 to 31.

32.2 The Supplier must not retaliate against any of the Supplier Staff who in good faith reports a breach listed in clause 32.1.

33. Resolving disputes

33.1 If there is a dispute between the Parties, their senior representatives who have authority to settle the dispute will, within 28 days of a written request from the other Party, meet in good faith to resolve the dispute.

33.2 If the dispute is not resolved at that meeting, the Parties can attempt to settle it by mediation using the Centre for Effective Dispute Resolution (CEDR) Model Mediation Procedure current at the time of the dispute. If the Parties cannot agree on a mediator, the mediator will

be nominated by CEDR. If either Party does not wish to use, or continue to use mediation, or mediation does not resolve the dispute, the dispute must be resolved using clauses 33.3 to 33.5.

33.3 Unless the Buyer refers the dispute to arbitration using clause 33.4, the Parties irrevocably agree that the courts of England and Wales have the exclusive jurisdiction to:

(a) determine the dispute;
(b) grant interim remedies;
(c) grant any other provisional or protective relief.

33.4 The Supplier agrees that the Buyer has the exclusive right to refer any dispute to be finally resolved by arbitration under the London Court of International Arbitration Rules current at the time of the dispute. There will be only one arbitrator. The seat or legal place of the arbitration will be London and the proceedings will be in English.

33.5 The Buyer has the right to refer a dispute to arbitration even if the Supplier has started or has attempted to start court proceedings under clause 33.3, unless the Buyer has agreed to the court proceedings or participated in them. Even if court proceedings have started, the Parties must do everything necessary to ensure that the court proceedings are stayed in favour of any arbitration proceedings if they are started under clause 33.4.

33.6 The Supplier cannot suspend the performance of the Contract during any dispute.

34. Which law applies

This Contract and any issues arising out of, or connected to it, are governed by English law.

APPENDIX A - VARIATION REQUEST FORM

Contract / Project Title: Contract / Project Ref No (FS /FSA No):
Full Description of Variation Request: A full justification and impact assessment including any supplementary evidence must be provided. Any supporting information should be appended to this form.
Area (s) Impacted: - Price ☐ Duration ☐ Price & Duration ☐ Scope of work ☐ Key Personnel ☐ Other ☐
Requester: Signature: Team / Organisation Date:
Supplier Contact Details Supplier Name : Contact Name : Contact Address : : Telephone No : Email Address :
FSA Use Only (Business Area) Amount Approved: Authorised By:- ☐ Cost Centre Manager ☐ Investment Board

Signed : Date of Approval: **Please submit this form to** fsa.procurement@food.gov.uk
Procurement Use Only (confirm contract allows for requested variation) Variation Request No: Variation Request Approved by: Date of Approval:
On full approval of this Request for Variation, Procurement will produce a Variation Form for agreement and approval by both parties to append to the Agreement / Contract.

APPENDIX B VARIATION FORM

PROJECT TITLE:

DATE:

VARIATION No:

BETWEEN:

The Food Standards Agency (hereinafter called "the Client") & SUPPLIER (hereinafter called "the Supplier")

1. The Contract is varied as follows:

Contract x

2. Words and expressions in this Variation shall have the meanings given to them in the Framework.

3. The Contract, including any previous Variations, shall remain effective and unaltered except as amended by this Variation.

SIGNED:

For: The Client	For: The Supplier
By:	By: . . . . .
Full Name:	Full Name: . . . . .
Position:	Title: . . . . .
Date:	Date: . . . . .