Minutes

Minutes of 104th meeting

MINUTES OF THE MEETING OF THE ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD (ACMSF) - HYBRID MEETING HELD ON 19th OCTOBER 2023 (ONE-HUNDRED AND FOURTH MEETING)

Present:

Chair: Prof. Dan Tucker

Members:

Prof Bill Keevil

Prof Peter McClure

Mr Alec Kyriakides

Mrs Ann Williams

Miss Heather Lawson

Dr Jane Gibbens

Prof Francis Butler

Dr Nicol Janecko

Dr Rohini Manuel

Prof Linda Scobie

Dr Edward Fox

Mr Martin Briggs

Dr Wayne Anderson

Prof Cath Rees

Dr Dragan Antic

Prof. Andrew Page

Dr Inaki Deza-Cruz

Ms Adri Bester

Dr Roberto Vivancos

Departmental representative:

Dr Stephen Wyllie (APHA)

Dr Lesley Larkin (UKHSA)

Secretariat:

Dr Anthony Wilson

Dr Elaine Pegg

Dr Johanna Jackson

Ms Azuka Aghadiuno

Presenters:

Dr Gary Barker

Dr Francesca Hodges

Prof. Sarah O’Brien

Members of the public: see Annex 1.

1. **Chair’s introduction**

1.1 The Chair welcomed members of the Committee and members of the public to the 104th meeting of the ACMSF. Prof. Dan Tucker chaired the meeting as Prof Keevil was unwell and was unable to attend the meeting in-person. He also welcomed Dr Gary Barker (Chair of the Botulinum Neurotoxin-Producing Clostridia subgroup, who presented agenda item 7, a discussion of the Report on Botulinum Neurotoxin-Producing Clostridia), Dr Francesca Hodges (Innovate UK, who presented agenda item 8, a presentation on 'Phage use in food production') and Prof. Sarah O'Brien (Newcastle University who presented agenda item 12, an update on the IID3 project).

1.2 As part of the meeting was opened to the public, the Chair mentioned that a full set of papers had been made available to members of the public via the ACMSF webpage.

2. Apologies for absence

2.1 Apologies from Gauri Godbole.

3. Declaration of interests

3.1 The Chair asked members if they wished to declare any potential conflicts of interest associated with the agenda items to be discussed.

3.2 No declaration was made.

4. Minutes of the 103rd meeting

4.1 A Committee member asked for a correction on page 8 section 7.2. They stated it is not about the phage being in food it is the regulatory framework around the use of phage in food products.

4.2 A Committee member stated that they sent through typing errors that were not captured in the minutes.

4.3 A Committee member asked for an amendment to page 5. To change a bullet point stating that Dr Stephen Wyllie "was unable to provide a response" be changed to "unable to provide a response at this time".

4.4 A Committee member highlighted that at the bottom of page 13 it states there is no plan for whole genome sequencing. This is not the case; it should say there is no metagenomic or direct whole genome sequencing planned for IID3.

4.5 Subject to the corrections listed above, members approved the minutes of the 103rd meeting as an accurate record and agreed that they should be posted on the ACMSF website **ACTION.**

5 Matters arising (ACM/1391)

5.1 ACM/1391 provided a summary of actions on matters arising from previous meetings. Dr Anthony Wilson reported that:

· The minutes from the 102nd meeting are now available on the ACMSF website.

· Several outstanding queries to APHA had been responded to via email prior to the meeting.

· The horizon scanning summary paper had been circulated prior to the meeting.

· In response to a query from a Committee member at a previous meeting around the regulations on the use of phage as a bio preservative in foods, a presentation by Francesca Hodges from Innovate UK has been arranged for this meeting entitled 'The use of phage in food production'.

· The requests made by the Committee on the formatting of the EFIG papers would be discussed at the next EFIG meeting on the 06/12/23.

· In response to a query on if a risk assessment on nisin had been considered by the FSA, the Committee were informed that an application (RP42) for use of Nisin in egg analogues (liquid and solid) will be reviewed by the AMR subgroup at the next meeting.

· Several queries for FSA policy were discussed with the Secretariat at a meeting on the 06/07/23. Policy provided the following responses to the queries.

o In relation to a recommendation that FSA highlight the importance of temperature control in consumer food hygiene campaigns, together with adherence to Use By dates, policy responded that they have taken this action on board and are happy to reflect in advice to consumers. They noted that advice on temperature control and use by dates are routinely factored into routine plans for consumer messaging. Recent examples of cold chain related messaging include power cut advice, and advice to university freshers which had a particular focus on use by dates.

o In relation to a recommendation that FSA guidelines should be slightly modified to include in the control actions “a combination of controlling factors which can be shown consistently to prevent toxin production by non-proteolytic *C. botulinum*”, policy confirmed that the action had been taken on board and that guidance is intended to be revised and is part of policies ‘100-day plan’. However, with the Report on Botulinum Neurotoxin-Producing Clostridia pending it was decided that the guidance should be review after the publication of the report.

o In relation to a recommendation from the Committee that more communication is needed to consumers on the risks of buying from unregulated food producers, policy highlighted several areas of work currently underway to address the risk from unregulated food producers. These included a recent paper on the cost of living and work being carried out by the Achieving Business Compliance (ABC) programme.

o In relation to a recommendation that that a food safety campaign be considered to highlight the need for proper handwashing, policy highlighted two recent research projects on this area: Kitchen Life 2 and handwashing behavioural trials. They will be preparing recommendations from these reports and will keep in mind the suggestion from the Committee when reviewing advice.

6. Committee update

6.1 Update on the AMR working group:

· Prof. Bill Keevil, as Chair of the AMR working group, gave an update on the group’s latest work.

· The last working group meeting was held on 12/09/23 .

· The issues considered during this meeting included:

o Presentation on EUCAST – an International Committee for Standards in Antimicrobial Susceptibility Testing: breakpoints, methods and guidance *Gunnar Kahlmeter, Head of EUCAST Development Laboratory and EUCAST Technical Data Co-ordinator and Webmaster*

o Update on development of next AMR National Action Plan (2025-2029): Food commitments and deliverables *Kathryn Callaghan, Food Standards Agency*

o Use of AMR terminology used in FSA reports *John Threlfall, Retired formerly Protection Health England*. An issue has arisen concerning the use of antimicrobial resistance (AMR) terminology in FSA research and survey reports. At

the April 2023 meeting of the AMR working group, it was agreed to convene a small group to pull together an initial set of definitions for the full group to consider. The specific action for this group was '*to consider defining specific AMR-related terms including their applicability in different situations'.* The progress of group was discussed with the working group during this meeting.

o Approach to assessing detriment of AMR genes in food risk assessments *Wioleta Trzaska and Paul Cook, Food Standards Agency*. Currently no framework has been developed in FSA risk assessments for assessing the severity of detriment resulting from exposure to microorganisms carrying specific AMR genes or combinations of genes or to phenotypic findings of resistance. One of the approaches would be to adapt WHO Critically Important Antimicrobials for Human Medicine List (CIA), as a reference when assessing severity of detriment. WHO's CIA list identifies antimicrobials used in animals that might present potentially higher risk to human. WHO uses criteria to categorise antimicrobials as Critically Important, Highly Important, or Important. The use of this approach was discussed by the working group.

· Date of next meeting will be **late January 2024**

7 Report on Botulinum Neurotoxin-Producing Clostridia (Gary Barker)

7.1 Dr Gary Barker presented the findings from the report.

7.2 Members discussed the ACMSF report produced by the Botulinum Neurotoxin-Producing Clostridia working group.

7.3 A Committee member highlighted an on-going Botulism outbreak in France and asked if FSA, alongside UKHSA, intend to send around a circular to small restaurants in the UK to remind them of the risks. The Secretariat responded that there is some guidance previously produced by the FSA, but we can review and get back to the Committee **ACTION**

7.4 A member suggested there is significant increase in artisan products which can lead to situations where botulism can occur including small scale bottling of products. Instruction or advisory guidance should go to producers but also inspectorate need training to spot the high risks associated with these activities. Dr Gary Barker responded that tracking is important with epidemiological quick links to cases and the first day and half being a crucial time for risk assessment. He suggested more sharing and coordination are essential.

7.5 A Committee member added that UKHSA are happy to take discussion forward in the matter of surveillance. It is a case of working closely with colleagues in FSA and relevant stakeholders to get response options in place to give the best possible risk communication measures.

7.6 The FSA policy representative highlighted that at least one incident in 2019 was dealt with a fast, stand-up response but agreed things can always improve and be learnt and incorporated for future.

7.7 A member raised the concern of the level of expertise needed highlighting and that it should be reported back to the research funders, such as BBSRC, to encourage a minimal level of research. A member responded that, in the past regarding expertise, the Institute of Food Research has been utilised. This is now part of Quadram and is there still a repository in that organisation. Another Member explained that the research programme had been cut, but it is limited to commercial testing in commercial labs, a collection is there and will be kept but new research is not on-going in the same way.

7.8 A member highlighted in the conclusion, it is stated that botulinum neurotoxin encoding genes have not been shown to form botulinum neurotoxin and have not been associated with foodborne Botulism. The conclusion goes on to say that a close eye should be kept on this. The committee member asked if this is going a step too far and suggested we should prioritise cases of Botulism and tracing. A working group member responded that they intended to raise awareness of monitoring research in that area.

7.9 A member suggested an amendment to the report, asking that Table 7 be repeated as well as the proteolytic clostridium table as these are useful for the practitioners. Also asked for footnote on the non-proteolytic report which comes from text on page 50 explaining the sensors to z values **ACTION.**

7.10 A Committee member asked for an update on the period of consultation Dr Gary Barker explained that some responses have been received and for efficiency wanted to decide what to look at with everyone in attendance at the plenary meeting and decisions will be made in due course.

7.11 Chair thanked Dr Gary Barker and the team for their hard work with the Clostridia report.

8 **Presentation on Phage Use in Food Production. Dr Francesca Hodges, InnovateUK.**

8.1 Dr Hodges's presentation included an overview of where phage are used in food production, examples of companies and applications of the technology, considerations for the regulation of phage in industry and an overview of Food Safety Research Network Projects.

8.2 The Chair thanked Dr Hodges for the presentation and opened the meeting to questions or comments.

8.3 A Committee member asked what tests or checks are being done to demonstrate that a phage is safe and what is their environmental survivability – does it disappear or is it permanently in the environment? Dr Hodges replied that this is something that the community is exploring along with the policy makers and regulators and there's a lot of information in the literature about the immunogenicity of phage. Clinical trials and feed trials that have been carried out already and though efficacy has not been demonstrated consistently, safety has been and there have been next to no adverse events demonstrated. As to persistence in the environment, once a propagating host is no longer available to the phage they will degrade with exposure to UV or be washed away and break down. Unless you are engineering a 'super-phage' that can exist permanently in the environment or will adapt to any bacteria around it, it's not likely that they will persist forever.

8.4 A Committee member asked, regarding resistance; bacteria become resistant to phage quickly that potentially by the time you have a product on the market it has become ineffective? Dr Hodges commented that this was a valid point. Most commercial phage products, are not a mono-phage product but a cocktail of phage that have been specially formulated together. Committee member Prof. Cath Rees clarified the following points –

· On the safety issue, there have been a lot of safety trials associated with phage therapy and where there has been adverse effects there has been a recognised reason why that has happened. We have learnt from those adverse effects and in recent trials in humans and animals there have not been adverse effects.

· Persistence – a lot of evidence from ecology work has shown that phage are grazed by protozoa and disappear from the population, and they are recognised in the research as part of the carbon cycle.

· Resistance – They are going to be applied in a situation where you get longer term resistance of the target organism and the phage. Cocktails that are

targeting different sites are produced. You will get resistance to a single phage quite quickly due to mutation in that population. Often the target site is something that is necessary for that organism, but if you have multiple target sites then resistance in that population goes down dramatically.

8.5 A Committee member commented that due to the different issues with the food industry, the regulatory framework is going to be incredibly complex. Despite MHRA or VMD considering this, the FSA should be looking after this in the context of the food industry issues.

8.6 A Committee member asked about persistence of phage in the gut? Dr Hodges commented that it depends on the product it is applied to. If it is a product that would be cooked then the risk of it transferring to the gut is very low, or if to packaging that will then be washed. It seems unlikely that a phage would make it through the gastrointestinal system without being specifically formulated to do so and survive the acidic environment of the stomach and the immunogenic reaction. Committee member Prof. Cath Rees also commented that pH 2 (within the stomach) is very good at inactivating anything that is exposed to it. To deliver a phage to the gut you have to go through huge amounts of protective encapsulation to get through the system intact.

8.7 A Committee member commented that there have been successful studies at reducing infection using phage in chicken, but they never clear the chicken of the bacteria. They suggested that this may then lead to increasing the risk of mutation and if the target organism was cleared then you open a niche for another one to replace it. It was suggested that there needs to be more research done to look at this. Dr Hodges answered that not all antimicrobials necessarily clear an infection anyway, there will always be resistant mutants. You may have slightly more versatility when designing a phage cocktail but there will always be a risk of creating an environment where resistant mutants can exist. As for the niche, this was examined in some work on phage in vacuum packed pork packaging to remove spoilage organisms. The bacteria cause odour which put consumers off the meat but they don’t do anything harmful. The danger is if you remove the harmless bacteria that something may grow in its place. More information is needed to look at how best to optimise the use of phage in these sorts of situations.

8.8 A Committee member followed up on this point with a comment on how bacteria have evolved their defence systems. You may have a phage that locks onto a receptor that is relatively well conserved on a specific bacterium, but that bacteria had evolved a defence strategy. Is it therefore going to be a waste of

time targeting that? Dr Hodges answered that as phage is a natural predator of bacteria, as the bacteria evolve, the phage can overcome that. That's not helpful if you have a fixed phage product but you could 'train' the phage to seek the mutant bacteria which makes them a more attractive option for the longevity of antimicrobial approaches. For example, the European Medicines Agency (EMA) has recently adopted scientific guidance for the use of phage in veterinary medicine. However, this allows multiple phages to be considered as one product. What is required is development of phage products and monitoring approaches for sustained effectiveness. Another Committee member noted that clearing everything from a product is less important as it is rarely achieved. Reduction in the probability of infections transmitted through the food chain is needed. Phage rarely clears infection but reduces microbial burden to allow the immune system to catch up.

8.9 A Committee member, commented that from a public health perspective, we have foodborne pathogens that are 'endemic' - that is that we live with them, and we are not in a position to be able to eliminate them, so we reduce the burden. For every human infection there is a dose response and so to reduce that dose is a win from public health side.

8.10 A Committee member commented that VMD is involved in regulating phage and asked if it was also the remit of the FSA and the equivalent feed additives process. They asked is there any sort of direction that they would like to see in terms of regulation? The Secretariat replied that momentum is building in this area.

8.11 The Chair thanked Dr Hodges for the presentation and the fascinating discussion and closed this agenda item.

9. AOB

9.1 Attention was brought to some circulated information papers, updates from other committees, and items of literature.

9.2 A Committee member made a request that acronyms are defined in the reports from the other committees **ACTION**.

9.3 A Committee member asked that *Yersinia* could be included in the items of literature paper **ACTION**.

9.4 The Chair paid tribute to the hard work and dedication of Ade Adeoye and the many years that he spent on the Secretariat until he moved to FSA Policy in Jan

2023. The Chair invited members to recognise his excellent service, thank him and wish him all the best in his future endeavours.

10. Public Q+A

10.1 The Chair asked if any members of the public or representatives of different organisations had any questions.

10.2 Karin Goodburn (Chilled Food Association) asked the FSA for clarity on the legal situation in the UK on the use of bacteriophage. She also raised a number of concerns using the term bio preservative.

10.3 Karin Goodburn (Chilled Food Association) asked for clarity on what the next steps were for the Botulinum report. Dr Gary Barker, Chair of the working group who produced the report, explained that the aim was for the final reports to be submitted at around Christmas time. Dr Barker confirmed that his group report would be very focussed around risk assessment. The Secretariat also stated there would be a response from the FSA as well as the Committee and the Secretariat in response to next steps in early 2024.

10.4 Karin Goodburn commented that there were items in current FSA guidance, that EHOs are referring to , which differs to recommendations in the report. The FSA policy representative responded that she appreciated Karin’s questions, and they will be considered. However, a definite timeline cannot be given, it will not be ignored but there are other priorities, but the report will be taken into consideration, and they will see where the guidance can be improved.

10.5 The Chair thanked the members of the public, members of the Secretariat and observers from different institutions and brought the public session of the meeting to a close.

11. Update on emerging issues - *Reserved business*

12. Update on IID3 - *Reserved business*

Annex 1

Observers:

Paul Cook

Mike Peck

David McDowell

Gail Betts

Gary McMahon

Ali Aitchison

Karin Goodburn

Anna Zarasvand

Helen Davies

Stephen Batchford