RCloud Tasking Form – Part B: Statement of Requirement (SoR)

Title of Requirement	Developing novel antibiotic therapies
Invitation to Tender No.	DSTLX-1000165473
SoR Version	1

1.	**Statement of Requirements**
1.1	**Summary and Background Information**
	Summary [REDACTED] group at the University of Exeter have developed a novel experimental approach based on microfluidics and microscopy that allows for the identification and investigation of individual bacteria surviving antibiotic treatment and thus posing a serious threat to human health. This experimental platform has been successful implemented for the evaluation of antimicrobials (antibiotics and bacteriophage) against Gram-negative pathogens including *E. coli*, *P. aeruginosa* and *B. thailandensis*. Dstl would like to continue to access this platform to evaluate novel combination therapies. **Background** Novel therapies for the treatment of infections with the biothreat pathogens are warranted, to ensure that our armed forces are suitably protected upon operations. Combination therapy approaches are being investigated as an avenue for improved treatment options, particularly with the increasing threat of antimicrobial resistance. [REDACTED] group at the University of Exeter have developed a novel experimental approach based on microfluidics and microscopy that allows for the identification and investigation of individual bacteria surviving antibiotic treatment and thus posing a serious threat to human health. This experimental platform has been successful implemented for the evaluation of antimicrobials (antibiotics and bacteriophage) against gram-negative pathogens including *E. coli*, *P. aeruginosa* and *B. thailandensis*. In addition, this platform has been developed to evaluate the response of *E. coli* to bacteriophage down to the level of the individual cell (manuscript under revision in *PLoS Biology*). This has also been further expanded to enable the characterisation of the uptake and efflux of antibiotic compounds in individual *E. coli* and *P. aeruginosa* cells which is paramount for understanding whether the drug in use can reach the target within all cells in the infecting population. The group has population-level preliminary evidence that ciprofloxacin treatment synergises with the temperate phage ØBp-AMP1 resulting in a reduction in the concentration of ciprofloxacin required to inhibit growth of *B. thailandensis*. However, the heterogeneity within the *B. thailandensis* population in the response to such combination therapy and other combination therapies facilitated by efflux inhibitors remains to be elucidated and this is paramount to ensure complete eradication of the pathogenic population. Further research is warranted to understand the mechanics at the single cell level, to ensure that the most appropriate and efficacious combinations are investigated and subsequently brought into Dstl for further evaluation.

1.2	**Requirement**
	The research assistant that will be contracted to [REDACTED] group at the University of Exeter will further develop this microfluidics and microscopy platform to: 1) Evaluate the response of *B. thailandensis* to both antibiotics and phage as sole and combination therapies. 2) Determine the accumulation of both antibiotics and phage within individual *B. thailandensis* cells.
1.3	**Options or follow on work**
	Submission of 2 x iCASE PhD studentship proposals but further proof-of-concept data is required to strengthen/support these applications.

1.4	Deliverables & Intellectual Property Rights (IPR)					
Ref.	**Title**	**Due by**	**Format**	**Expected classification (subject to change)**	**What information is required in the deliverable**	**IPR Condition**
1	Quarterly technical reports	T0+3 months	Presentation and/or written report	O	Quarterly report to include: • Update on technical progress • Progress report against project schedule.	DEFCON 705 shall apply
2	Annual report	T0+12 months	Presentation and/or written report	O	Annual report to include: • Update on technical progress • Progress report against project schedule. Detail method development and analytical approach sufficient to inform joint publications and in preparation for future regulatory strategies.	DEFCON 705 shall apply