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

Title of Requirement	*B. thailandensis* CPS analysis and AAC development
Requisition No.	**RQ0000009538**
SoR Version	**0.1**

1.	**Statement of Requirements**
1.1	**Summary and Background Information**
	B. thailandensis E555 capsular polysaccharide (CPS) will be isolated and analysed via NMR with and without the addition of monoclonal antibodies or antibody-antibiotic conjugate (AAC), to evaluate binding mechanisms and binding efficiency. Then optional follow on studies include: further CPS NMR analysis; enhancement of AAC and generation of antibody-glycan immune stimulating conjugate. An antibody drug conjugate (AAC) containing a *Burkholderia pseudomallei* anti-CPS monoclonal antibody (mAb) is being developed by Mologic (DSTLX-1000161420). In order to optimise the development of this AAC and inform antibody engineering, more information is needed on the binding properties of the native and AAC mAbs to CPS. This can be evaluated by NMR to elucidate the mechanism and efficacy of mAb binding to the CPS and identify key carbohydrates and amino acids resides required for the interaction. *B. thailandensis E555* is a non-pathogenic strain closely related to pathogenic *B*. *pseudomallei*, which is the causative agent of melioidosis. *B. thailandensis E555* capsular polysaccharide (CPS) has been found to be undistinguishable from CPS of the pathogenic strains and can therefore be produced as a safe alternative for immunological studies
1.2	**Requirement**
	Task 1.1 CPS generation and initial NMR studies - Production of >15 mg *Burkholderia thailandensis E555* capsular polysaccharide (CPS). - Characterisation of CPS product by NMR and GPC fractionation. - Determine mAb binding to GPC fractions of CPS and determine best fraction/binding conditions inform future NMR experiments. - Determine mAb binding to AAC (provided by Mologic) and comparison with binding mAbs (provided by Dstl) - Perform STD NMR study to evaluate CPS bound to mAb or mAbs conjugate. The supplier will be required to provide quarterly report and annual reports. Details are captured in the Deliverable Table (Section 1.6)

	The supplier can chose if they provide the quarterly and annual reports as a virtual presentation or a formal report.
1.3	**Options or follow on work** *(if none, write 'Not applicable')*
	Options may be picked up at any time after 6 months. The supplier will be required to provide quarterly technical progress reports and annual reports for these optional tasks. Details are captured in the Deliverable Table (Section 1.6) **Task 1.2 CPS generation and further NMR studies** - Repeat purification of the CPS to yield sufficient material for ongoing analysis. - Complete STD NMR study: CPS with mAb (provided by Dstl) & mAbs conjugate (Mologic). - Explore binding differences between unmodified mAbs or mAbs drug conjugates against CPS and bacteria killed cells (ELISA). - Rationalisation of data, difference in binding to CPS between mAbs and ADC, instruct on mAbs conjugates: ideal number of conjugates to maximise binding. **Task 1.3 CPS generation and further NMR studies** Repeat purification of the CPS to yield sufficient material for ongoing analysis. - Explore knowledge across towards development of ADC for alternative pathogen E.g. *Coxiella burnetii*, or *Yersinia pestis*. **Task 2.1 Enhancement of AAC** - Rationalisation of AAC and influence on the binding might require re-design of the construct with site specific modification achieved by glycan remodelling program. - CPS binding comparison, identification of key binding site & interference of the conjugate drug with the binding. - Chemoenzymatic remodelling of the ADC N-glycans followed by oxidation of the N-glycan fucose or galactose to generate a reactive aldehyde that can be successively targeted with simple reductive amination to install the desired conjugate molecule. Or galactose oxidase and tandem Knoevenagel–Michael addition conjugation chemistry. - Preparation of antibiotic equipped with cathepsin cleavable linker. - New ADC preparation and estimation of number of conjugated drugs**.** - ELISA (established in Task 1) and interaction studies with new AAC and purified CPS. - STD NMR studies and comparison of binding efficiency between mAbs (Dstl), AAC (Mologic), new AAC (Iceni). - Optimisation/enhancement of the existing AAC, test of cleavable linker guided by interaction study results. **Task 2.2 Further enhancement of AAC**

	- STD NMR studies and comparison of binding efficiency between mAbs (Dstl), ADC (Mologic), new ADC (Iceni). - Repeat purification of the CPS if further material needed. **Task 3.1 Generation of antibody-glycan immune stimulating conjugate** - Chemoenzymatic remodelling of the ADC N-glycans followed by oxidation of the N-glycan fucose or galactose to generate a reactive aldehyde that can be successively targeted with simple reductive amination to install the desired conjugate molecule. Or galactose oxidase and tandem Knoevenagel–Michael addition conjugation chemistry. - mAbs (provided by Dstl or BBI) conjugated with carbohydrate hapten 1, (3 different available) will include the preparation of carbohydrates hapten equipped with non-cleavable linker. - ELISA binding assay with CPS (Established in Task 1) and verify binding of new mAbs conjugate with hapten 1. - mAbs (provided by Dstl or BBI) conjugated with carbohydrate hapten 2, (3 different available) will include the preparation of carbohydrates hapten equipped with non-cleavable linker. - ELISA binding assay with CPS (Established in Task 1) and verify binding of new mAbs conjugate with hapten 2. **Task 3.2 Optimisation of antibody-glycan immune stimulating conjugate** - mAbs (provided by Dstl or BBI) conjugated with carbohydrate hapten 3, (3 different available) will include the preparation of carbohydrates hapten equipped with non-cleavable linker. - Elisa binding assay with CPS (Established in Task 1) and verify binding of new mAbs conjugate with hapten 3. - Summary of the ELISA binding results, selection of best candidate for future in vivo studies.
1.4	**Contract Management Activities**
1.5	**Health & Safety, Environmental, Social, Ethical, Regulatory or Legislative aspects of the requirement**
	HSE approved CL2 laboratories

1.6	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 monthsand every 3 months thereafter*	*Presentation and/or written report*	*3*	*O*	*Quarterly report to include but not limited to:* *• Update on technical progress* *• Progress report against project schedule.*
2	Annual report	T0+12 months	*Presentation and/or written report*	3	O	*Annual report to include but not limited to:* *• 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.*

1.7	**Deliverable Acceptance Criteria**
	All Reports included as Deliverables under the Contract e.g. Progress and/or Final Reports etc. must comply with the which defines the requirements for the presentation, format and production of scientific and technical reports prepared for MoD. Interim or Progress Reports: The report should detail, document, and summarise the results of work done during the period covered and shall be in sufficient detail to comprehensively explain the results achieved; a description of current substantive performance and any problems encountered and/or which may exist along with proposed corrective action. An explanation of any difference between planned progress and actual progress, why the differences have occurred, and if behind planned progress what corrective steps are planned. Final Reports: shall describe the entire work performed under the Contract in sufficient detail to explain comprehensively the work undertaken and results achieved including all relevant technical details of any hardware, software, process or system developed there under. The technical detail shall be sufficient to permit independent reproduction of any such process or system. All Reports shall be free from spelling and grammatical errors and shall be set out in accordance with the Statement Of Requirement (1) above

2	**Evaluation Criteria**
2.1	Method Explanation
	Direct award – Evaluation is based on technical compliance and affordability
2.2	Technical Evaluation Criteria
	The technical proposal should address requirements as set out in Section 1.2 - Confirmation that the proposal fully meets the Authority's Statement of Requirement. Pass/Fail
2.3	Commercial Evaluation Criteria
	The commercial evaluation shall be based on the following Pass / Fail questions: 1. Has the bidder submitted one (1) full proposal (Technical and Commercial) including all price detail, and has the bidder submitted one (1) Full Technical proposal which excludes all commercial price information? 2. Has the bidder submitted the proposal as a Firm price? 3. Are Labour rates and price as per the rates uploaded to RCloud? 4. Has the bidder submitted one (1) completed copy of RCloud Form Part C – Task Response Form? 5. Has the bidder completed DEFFORM 711 - Notification of IPR Restrictions? 6. Has the bidder completed a Statement Relating to Good Standing (SRGS)? 7. Has the bidder completed Research Worker forms as necessary?

	A fail on any of the above questions will result in your proposal being excluded from further evaluation and consideration. Additionally, the proposal will be evalutated on NAPNA principles (no acceptance no contract). The proposal should be priced in-line with the agreed framework (R-cloud) rates with all materials and T&S broken down