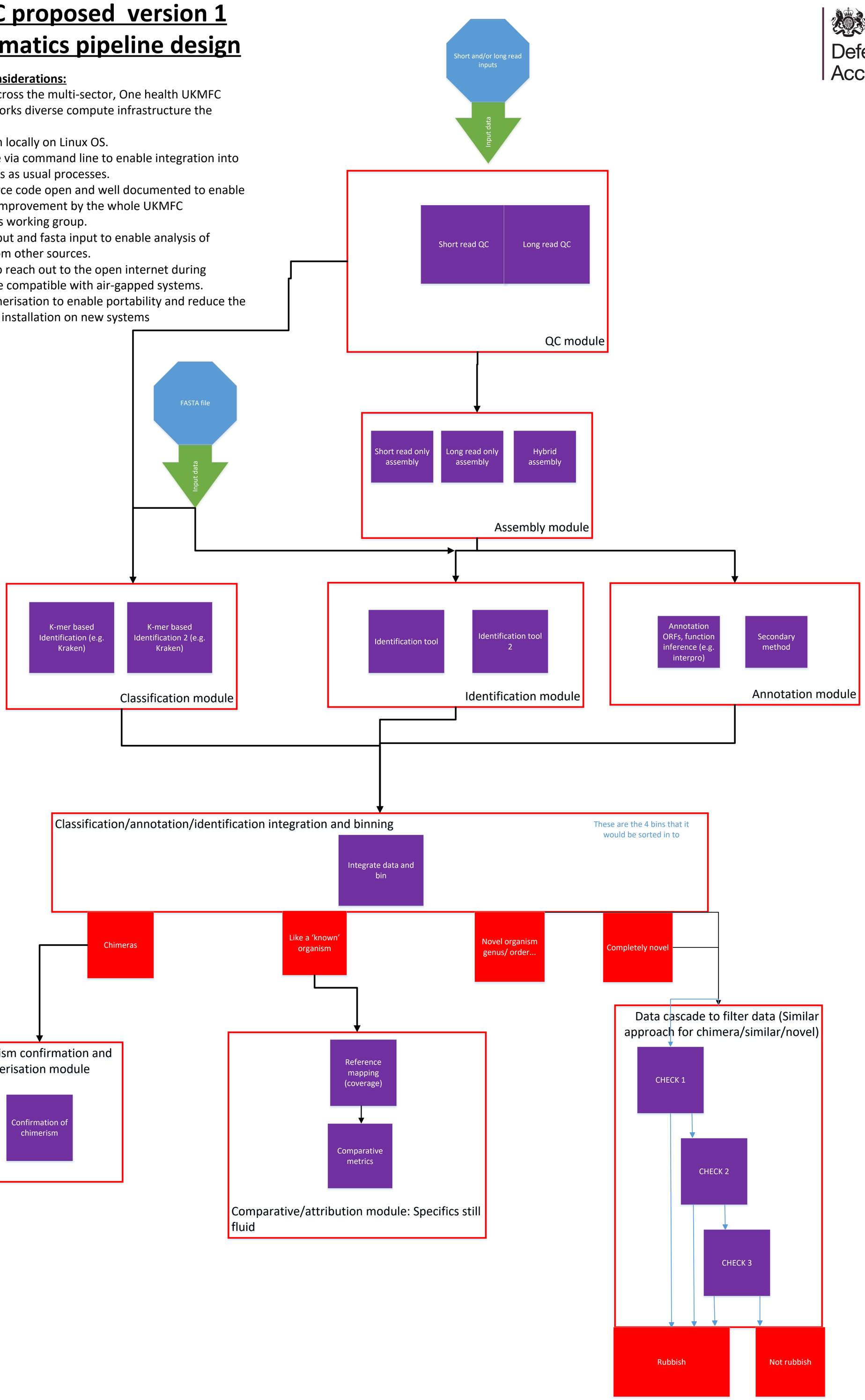
UKMFC proposed version 1 bioinformatics pipeline design

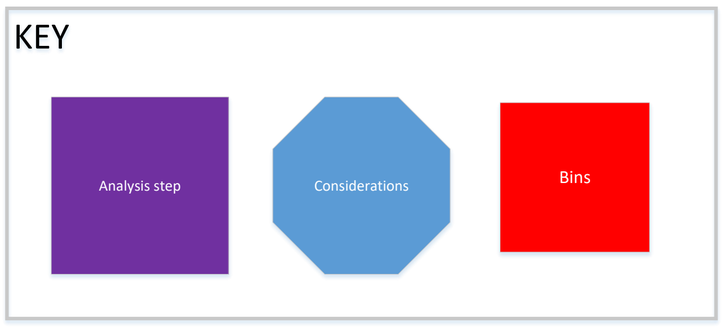
Defence and Security Accelerator

Main design considerations:

To enable use across the multi-sector, One health UKMFC laboratory networks diverse compute infrastructure the pipeline will:

- Be built to run locally on Linux OS.
- Be executable via command line to enable integration into wider business as usual processes.
- Have the source code open and well documented to enable scrutiny and improvement by the whole UKMFC bioinformatics working group.
- Have fastq input and fasta input to enable analysis of sequences from other sources.
- Not be able to reach out to the open internet during analysis i.e. be compatible with air-gapped systems.
- Utilise containerisation to enable portability and reduce the complexity of installation on new systems





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Identification of laboratory passage

This competition seeks to identify signatures of deliberate production and/or release of biological organisms. Technical approaches offer the potential to identify that the organism within a sample harbours phenotypic evidence of laboratory passage/growth (e.g. either at the epigenetic, transcriptomic, proteomic level). Previous research has highlighted the potential of this analysis technique for investigation of the misuse of biological materials (1, 2). For the identification of robust signatures, suppliers should consider using an environmental strain (i.e. one which has little or no previous laboratory culture) for passage experiments. It is anticipated that signatures would be identified following a relatively small number of culture "generations" during laboratory passage experiments (i.e. emerging following being repeatedly passaged less than 10 times).

1. Merkley ED, Sego LH, Lin A, Leiser OP, Kaiser BLD, Adkins JN, et al. (2017) Protein abundances can distinguish between naturally[1]occurring and laboratory strains of Yersinia pestis, the causative agent of plague. PLoS ONE 12(8): e0183478. https://doi.org/10.1371/journal. pone.0183478
2. Leiser OP, Blackburn JK, Hadfield TL, Kreuzer HW, Wunschel DS, Bruckner-Lea CJ. Laboratory strains of Bacillus anthracis exhibit pervasive alteration in expression of proteins related to sporulation under laboratory conditions relative to genetically related wild strains. PLoS One. 2018 Dec 17;13(12):e0209120. doi: 10.1371/journal.pone.0209120

Genetic Modification methods

In the Synthetic Biology era there is a wide range of described methods by which microbial agents may be modified. Two review papers are provided which detail such methods, though these should be considered as a brief introduction into this area rather than a systematic literature search and, as such, it should be understood that other modification methods (especially for viral agents) exist.

Proposals should seek to develop technology options that would identify genetic engineering conducted using as many of these methods as possible, with an aspiration that a technology option provides a definitive indication that an agent has been deliberately engineered. Where a definitive indication is not possible then a likelihood score could be provided as an alternative, though it would need to be made clear what criteria informed the final score.

1. Broothaerts, W., Jacchia, S., Angers, A., Petrillo, M., Querci, M., Savini, C., Van Den Eede, G. and Emons, H., New Genomic Techniques: State-of-the-Art Review, EUR 30430 EN, Publications Office of the European Union, Luxembourg, 2021, ISBN 978-92-76-24696-1, doi:10.2760/710056, JRC121847
2. Hwang J., et al. Mobile genetic element-based gene editing and genome engineering: Recent advances and applications, Biotechnology Advances, Volume 72, 2024, 108343, ISSN 0734-9750