Appendix 1

Key requirements and entry thresholds for a lead compound to enrol in the NADP Lead Development Voucher financing instrument

- The lead compound must concern a novel antibiotic or alternative therapeutic for the treatment of bacterial infections, as described in the NADP Research and Development Agenda. Preventatives, diagnostic tools, and enabling technologies will not be considered.
- The lead must target at least one pathogen from the WHO priority pathogens list for R&D of new antibiotics (http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/). Additional pathogens considered here include *Clostridium difficile, Streptococcus pneumonia*, and *Mycobacterium tuberculosis*.
- The lead development stage must lie between "having a validated hit ready to enter lead selection" and "the end of pre-clinical testing".
- A minimum of 4 of the following characteristics should be available about the antibiotic or alternative therapeutic lead involved, where more characteristics provide a higher chance of awarding:
    1. *Demonstrated understanding of the mode of action;*
    2. *Minimal inhibitory concentration (MIC) ≤ 32 µg/ml for Gram-negative pathogens or MIC ≤16 µg/ml for Gram-positive pathogens (or proven in vitro activity if MIC values cannot be measured);*
    3. *In vitro minimal bacterial killing dose for alternative therapeutic leads (i.e. 10 phages/bacterium);*
    4. *Demonstrated chemical or biological structure;*
    5. *Reasonable route of synthesis (or availability of product if natural-product derived);*
    6. *Activity against relevant resistant strains, if targeting a known mechanism;*
    7. *First data on stability, solubility, selectivity, and bioavailability;*
    8. *First data on haemolytic, cytotoxic, and/or immunogenicity data of alternative therapeutic lead;*
    9. *Enough starting material should be available upfront the study to complete proposed project.*