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, (medication) delivery devices, new formulations of existing therapeutics, 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.*