Mission – Public Health England

“To protect and improve the nation’s health and to address inequalities, working with national and local government, the NHS, industry, academia, the public and the voluntary and community sector.”
PHE - Porton

- emergency response capability
- high containment of pathogenic agents [CL2-CL4]
- diagnostic capabilities [RIPL]
- culture collection (CC of PHE)
- developmental production
- biopharmaceutical manufacture
- translational research
Translational Research Model

In vitro, in vivo, product development and clinical studies

Discovery
Applied research

Development
Translational research

Licensure

Flexible interactions with partners along the development pathway

Discovery → Industry

Academia/Govt/NforP

Past successes: Whooping cough, Meningitis, Anthrax, Plague, Dysport (cerebral Palsy), Erwinase (childhood leukaemia), Decontamination products.

Capabilities maintained for microbiological emergency response

Key role in UK Life Sciences Strategy
Infectious Disease Programmes

- **TB**
  - Vaccines
  - Antibiotics
  - Diagnostics

- **Toxins**
  - Botulinum
  - Clostridium
  - Immunotherapy
  - Diagnostics

- **Mening & Pertussis**
  - Correlates
  - Vaccines

- **Biosafety**
  - Detection
  - Decontam
  - HCAI/vCJD
  - Training

- **Animal Models**
  - Efficacy studies
  - Aerosol
  - Pathol/Imaging
  - Immunology

- **GxP**
  - Immune Assay
  - Clinical Trials
  - Assay Validation
  - Product release assays

- **Immune Modulation**
  - Inflammation
  - Adjuvants

- **Emerging Diseases**
  - Virology/Influenza
  - Bacteriology

- **Diagnostics Technology**
  - Diagnostics
  - Bio/Molecular

- **Medical Counter Measures**
  - NIAID
  - Anthrax

Developing Interventions with academia, Govt and industry
US projects at PHE Porton

Antibiotics, small molecules & therapies (A1, B1)
  Anthrax (C1)
  Plague (C18)
  Q fever (C19)
  Melioidosis (C19)
  Filoviruses (C20)

BARDA BIO-0001 (Melioidosis)
BARDA BIO-0004 (Anthrax)

Discovery
Pure research

Development
Translational research

Licensure

Anthrax (D1)
Melioidosis (D19)
Glanders (D19)
Multiple agents (D8, Dstl)
Orthopox (D4/D7, D18, E07) C03
Flu (E10)
Capabilities - Chemostat

Applications

- Multiple pathogens including *M. tuberculosis*
- Multiple parameters including growth rate and nutrient limitation

Rapid assay for drug evaluation
Live / dead fluorescence stains and flow cytometry

Defined populations:
- Live
- Dead
- Persistent
Step-wise evaluation of interventions

Provide rational information to support decisions in clinical trials

**Relevant in-vivo models for screening**
- Appropriate dose and route of challenge
- Robust and reproducible measures of efficacy

**Advanced in-vivo models**
- Predictive for humans
- Parallel studies with early clinical trials

*In vivo Models must be*
- Well characterised
- Predictive
- Use clear readouts

**Systems for pre-screen to minimise animal use (3Rs)**

**Clinical Trials**
Experimentally generated aerosols

Controlled aerosol delivery:
- Collison nebuliser
- range of animal species
- nose-only exposure <5 µm

Henderson apparatus controlled by AeroMP
Preclinical testing for TB

- Range of species.
- Immunogenicity and challenge studies.
- ACDP3 containment facilities: *in vitro, in vivo, ex vivo* studies.
- Large capability
  (largest TB vaccine evaluator in Europe – small animal models).
- Advanced NHP capability.
Clinically relevant mucosal delivery

Aerosol Route - TB Vaccine Delivery

- Three distinct functional profiles
- Antigen-specific cells increase at the mucosal surface following BCG vaccination
- Responses peak 1 week following Booster vaccination

Analysis of immune response using BAL

Cells isolated for flow cytometry & Polyfunctional T-cell analysis

Exclusion of Doublets, Dead cells, B cells & NK cells
Relevant and natural routes of challenge

Animal modelling capability to study Tick Vector competency:
Tick transmission studies with Hazara, CCHF, TBE viruses.
  • PHE PhD studentship [Liverpool – PHE HPRU]

Assessment of vector competence.
⇒ Ability to test interventions using a natural route of infection

Natural Transmission by airborne route

- Influenza
- Tuberculosis
In vivo CL4 facilities
• Haemorrhagic Fever viruses
  *Filoviridae*
  *Arenaviridae*

• Arboviruses
  *Flaviviridae*
  *Bunyaviridae*
  *Togaviridae*
  *Reoviridae*

• Orthopoxviruses
• Hantaviruses
• Henipaviruses

WHO Collaborative Centre for Viruses (Arboviruses & VHF)
Porton Down 1976
Ebola studies

• **In –vivo studies to test interventions:**
  - Pharmacokinetic studies.
  - Pathogenesis studies
  - Vaccine assessment.
  - Repeat drug dosing.
  - Safe system of administration.

• **Collaborations:**
  - West Africa deployment of staff trained in high containment
  - On-going R&D projects [immune responses in humans, vaccine trial]
New antigens:
- meningitis
- TB
- anthrax
- C. difficile

Correlates of protection:
- meningitis
- pertussis
- TB

Evaluation [clinical trials]:
- NVEC
- grants
- commercial

Evaluation in preclinical models:
[drugs, vaccines, etc]
- medical counter-measures
- TB
- ‘flu
- ......& many others....
PHE Porton: Unique Translational Research Capability

Translational R&D

Correlates of protection:
- meningitis
- pertussis
- TB

Animal model:
- range of species

Model design:
- aerosol challenge
- vaccine delivery
- high containment

Readouts:
- survival
- organ CFU
- immune response
- pathology
- clinical chemistry [PK]
- imaging

Evaluation in preclinical models:
[drugs, vaccines, etc]
- medical counter-measures
- TB
- 'flu
- ......& many others....
In life’ imaging – use of mobile scanner units

Approaches can be applied to any pathogen / intervention

‘In life’ imaging: CT