Imperial College London

EPSRC
Future Vaccine Manufacturing Research Hub

Advancing the manufacture and deployment of cost effective vaccines

Future Vaccine Manufacturing Research Hub

- Introduction to the FVMR Hub
- Aims and objectives
- Hub capabilities and initiatives
- Current partners
- Opportunities for interaction, partnerships and proposals
- Discussion

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Future Vaccine Manufacturing Research Hub

Introduction to the Hub

- The new Future Vaccine Manufacturing Research Hub at Imperial College London, has been established with £10 million (GBP) of funding from the UK Department for Health, administered by EPSRC.
- Incorporates research groups across Imperial College experiences in vaccine R&D, process engineering and manufacturing
- Linked to additional UK spokes with experience in formulation, computational modelling, process development and vaccine QA/QC (NIBSC)
- Established developing country vaccine manufacturer spokes, initially in India, Vietnam, Bangladesh, Uganda and China
- Looking to expand collaboration with additional partners.

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Future Vaccine Manufacturing Research Hub

Aims and objectives

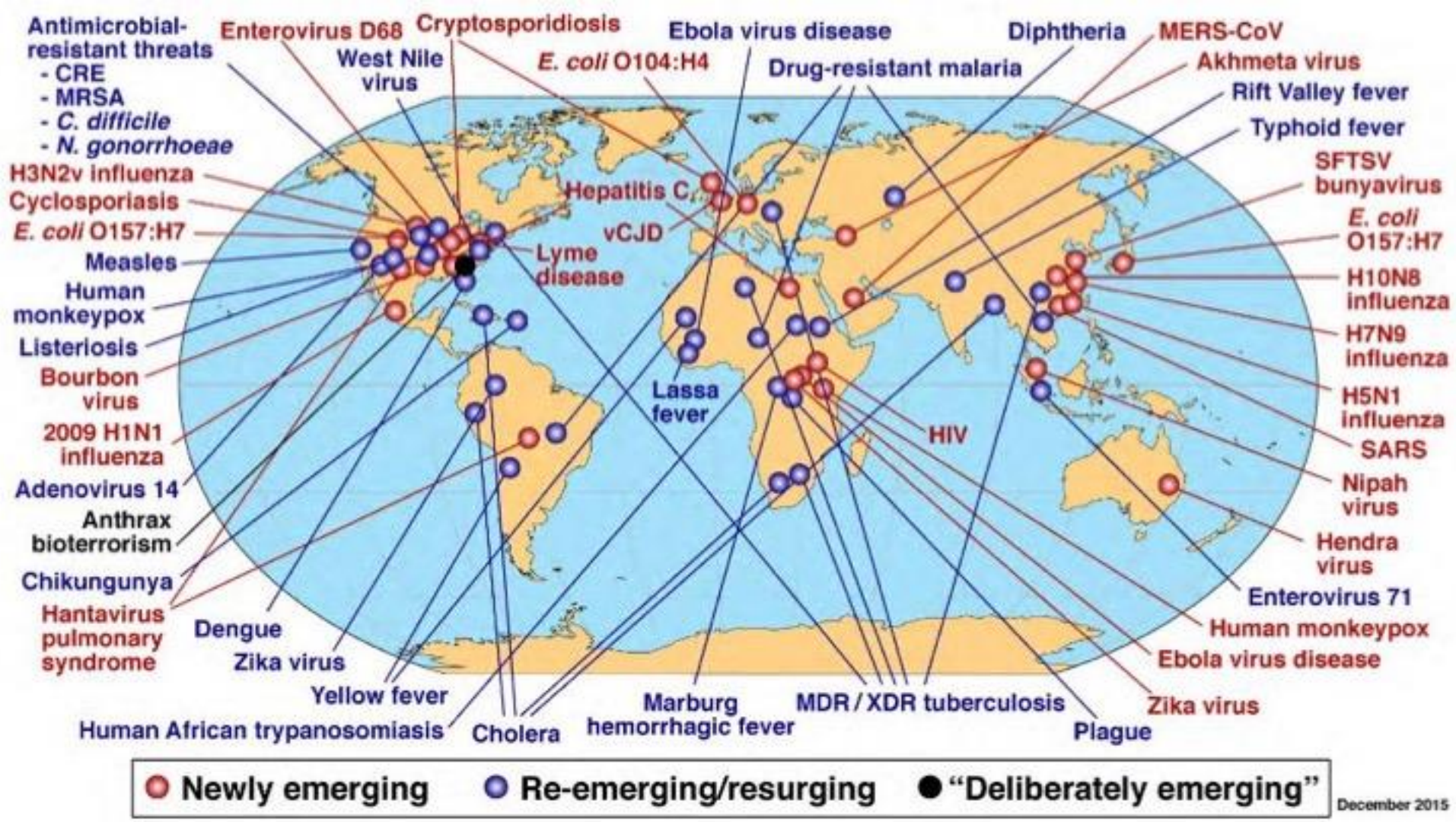
- We will adopt an integrated approach that will build on new developments in life sciences, immunology and engineering to address two key challenges

  - How to design production systems that can produce tens of thousands of new doses within weeks of a new threat being identified

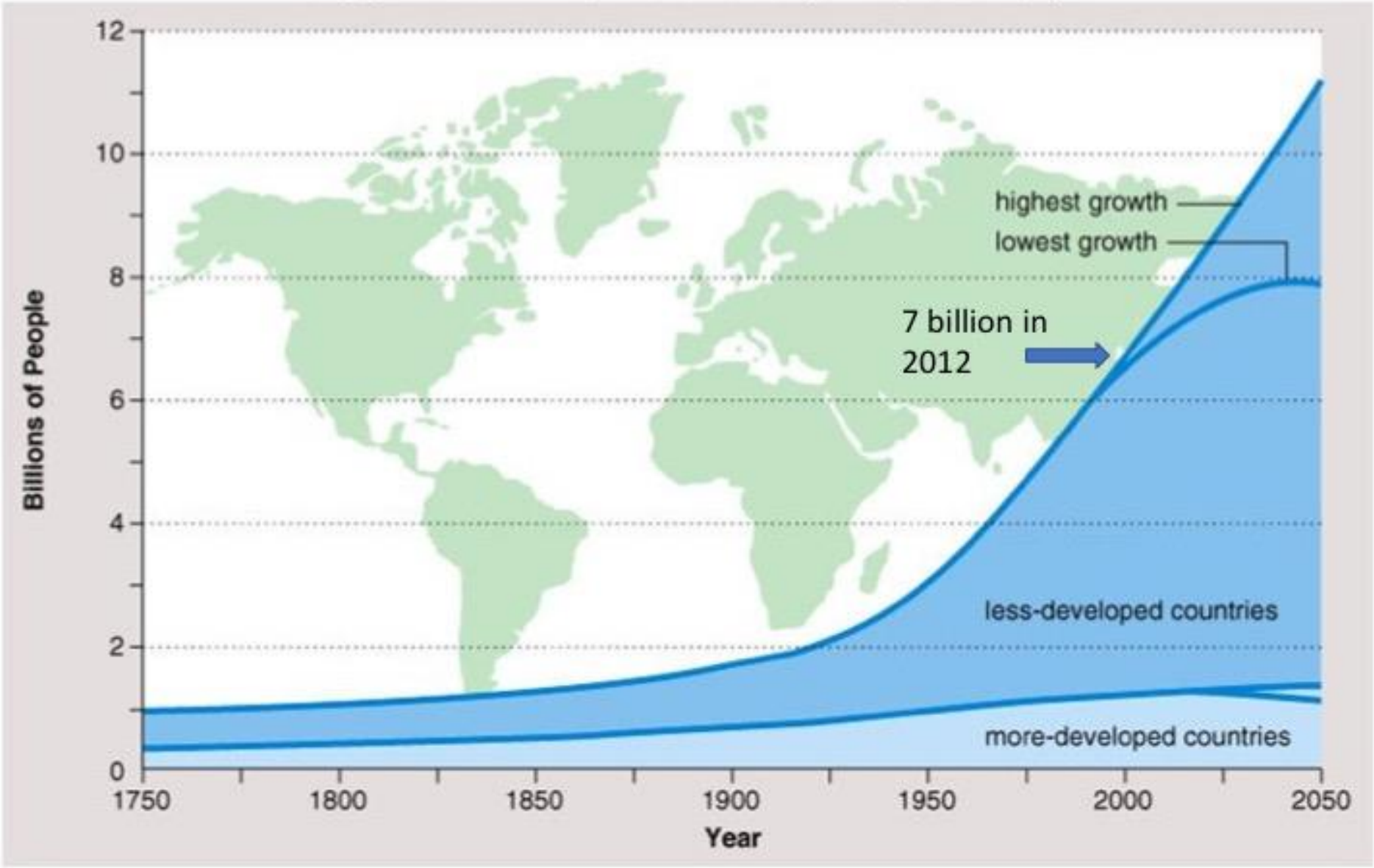
  - How to improve the way vaccines are manufactured, stabilised and stored so that existing and new diseases can be prevented effectively, and costs reduced

Goal: **advancing the manufacture and deployment of cost effective vaccines**

Responsive to the treat of emerging and re-emerging infections



Responding to developing world vaccine needs

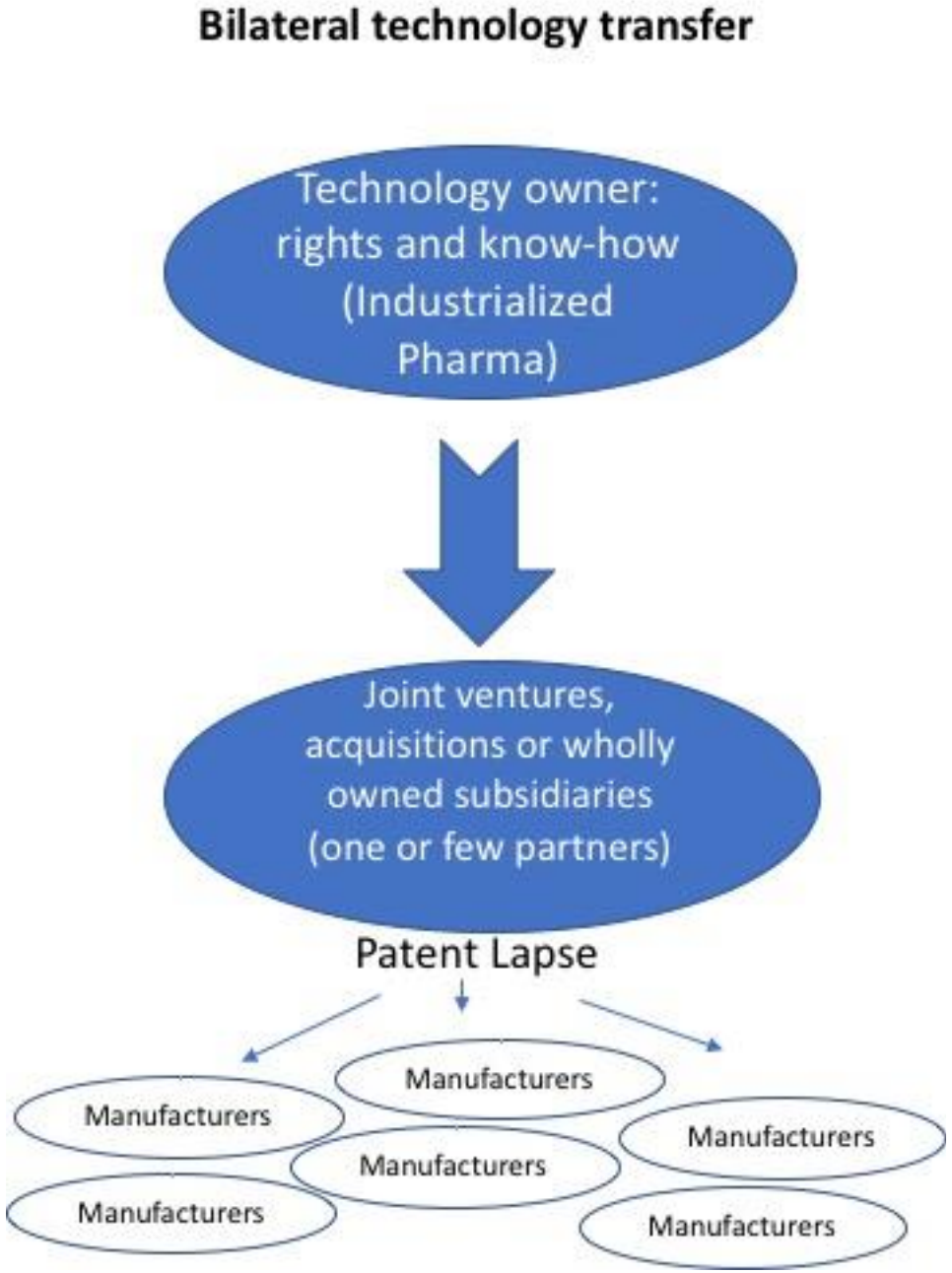


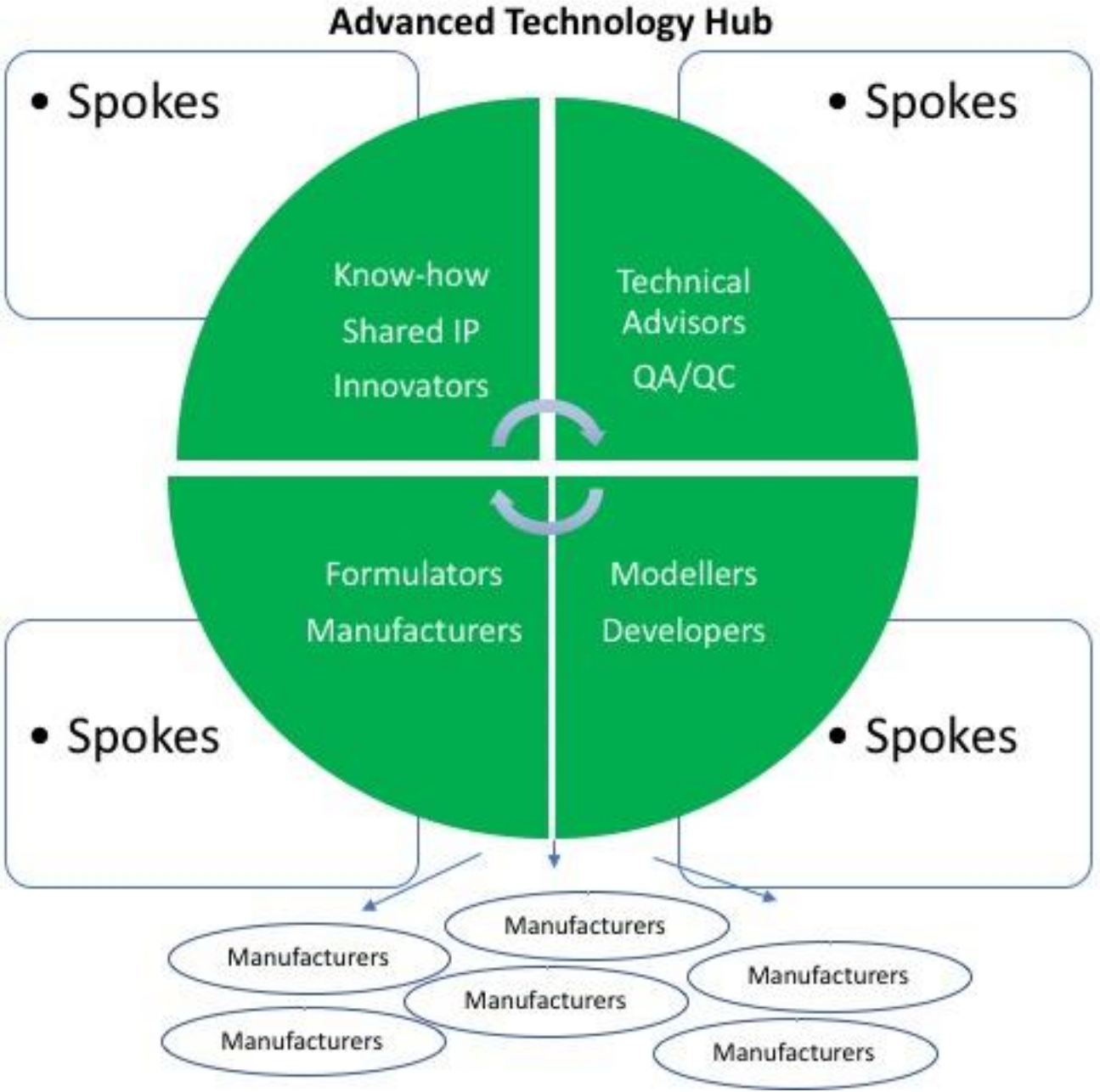
Identifying gaps in technology transfer

- Research and Development capacity to support technology transfer, develop novel vaccines, work around existing IP
- Vaccine specific modelling – manufacture, distribution, markets
- Business case/sustainability to support adoption, adapt to changing markets, respond to supply and demand
- Know-how – workforce (training, expertise, retention)
- Know-how in emerging technology (when to adopt or drop)
- Know-how in process optimisation
- QA/QC and regulatory affairs for new technologies and ultimately pre-qualification

Opportunity: leap-frog existing investments by exploiting emerging platforms

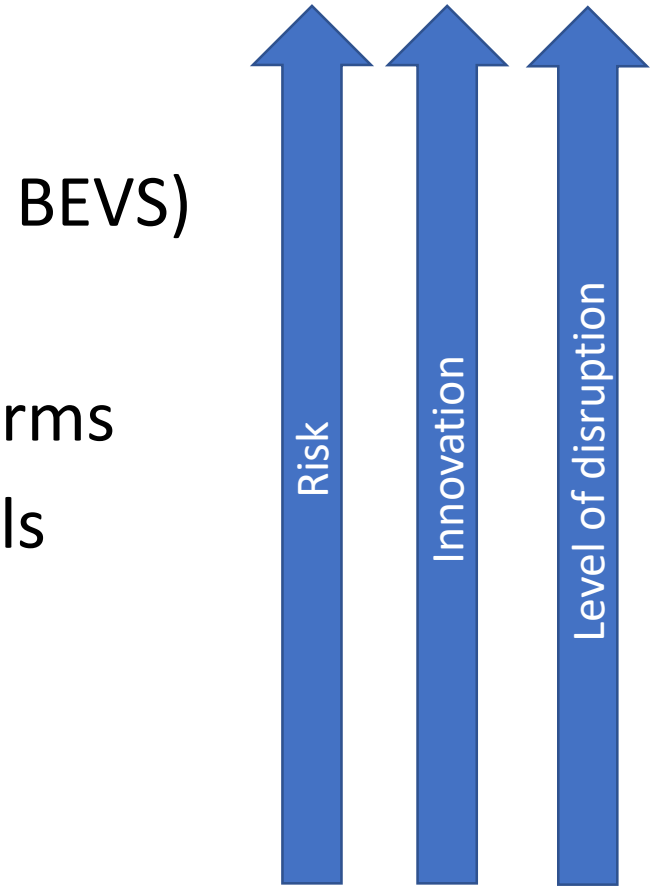
New model for Technology Transfer

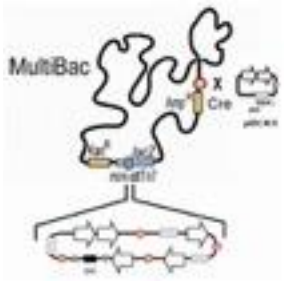


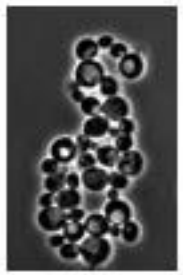


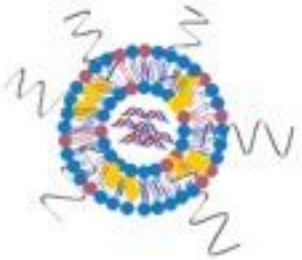
Engineering deliverables at multiple levels

- Replicon RNA vaccines
- Enhanced yeast expression platforms
- Insect cell-baculovirus expression system (IC- BEVS)
- Formulation for heat stabilisation
- Process optimisation of manufacturing platforms
- Vaccine specific modelling and decisional tools
- R&D training and support
- QA & QC support and training

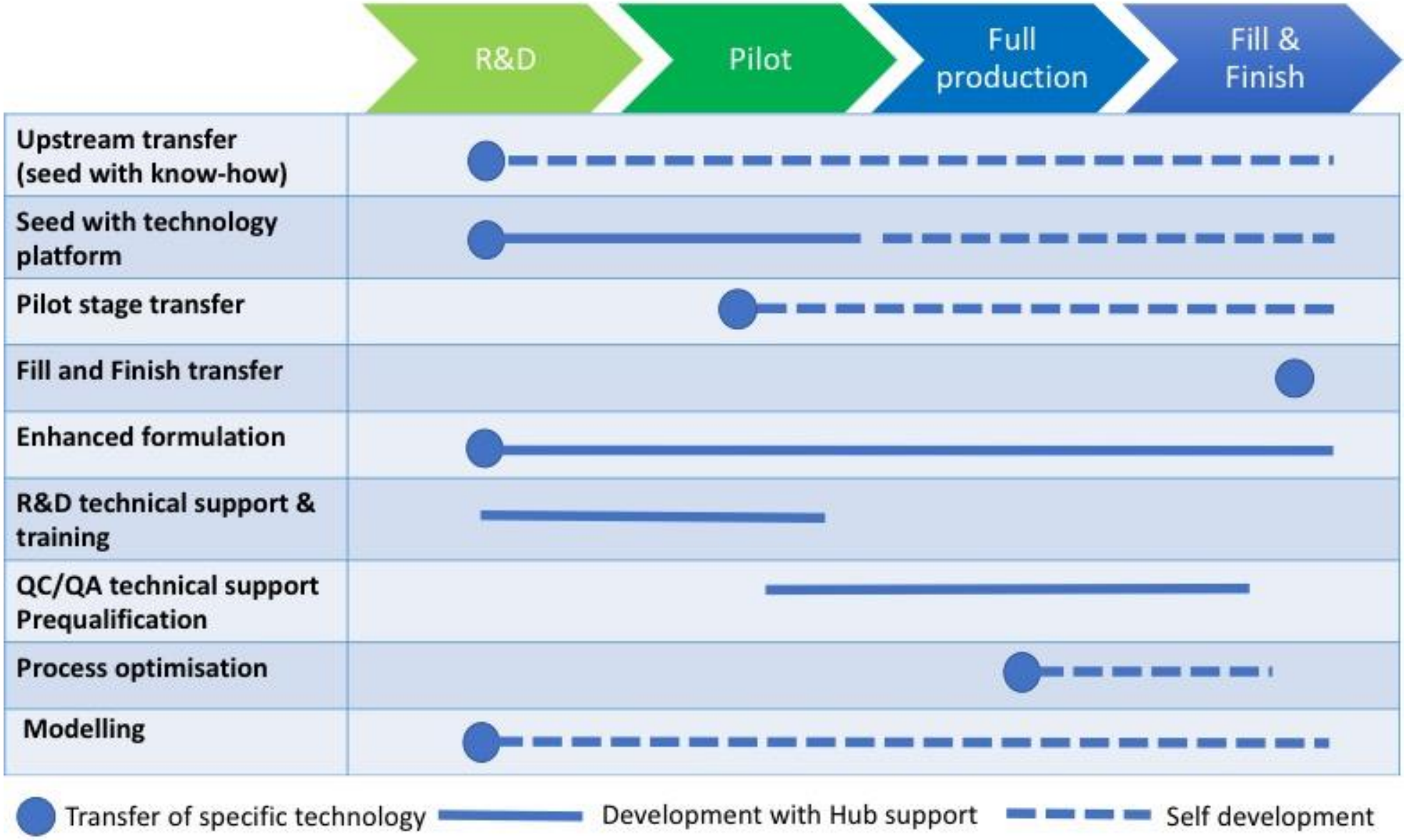








Developing appropriate partnership



Future Vaccine Manufacturing Research Hub

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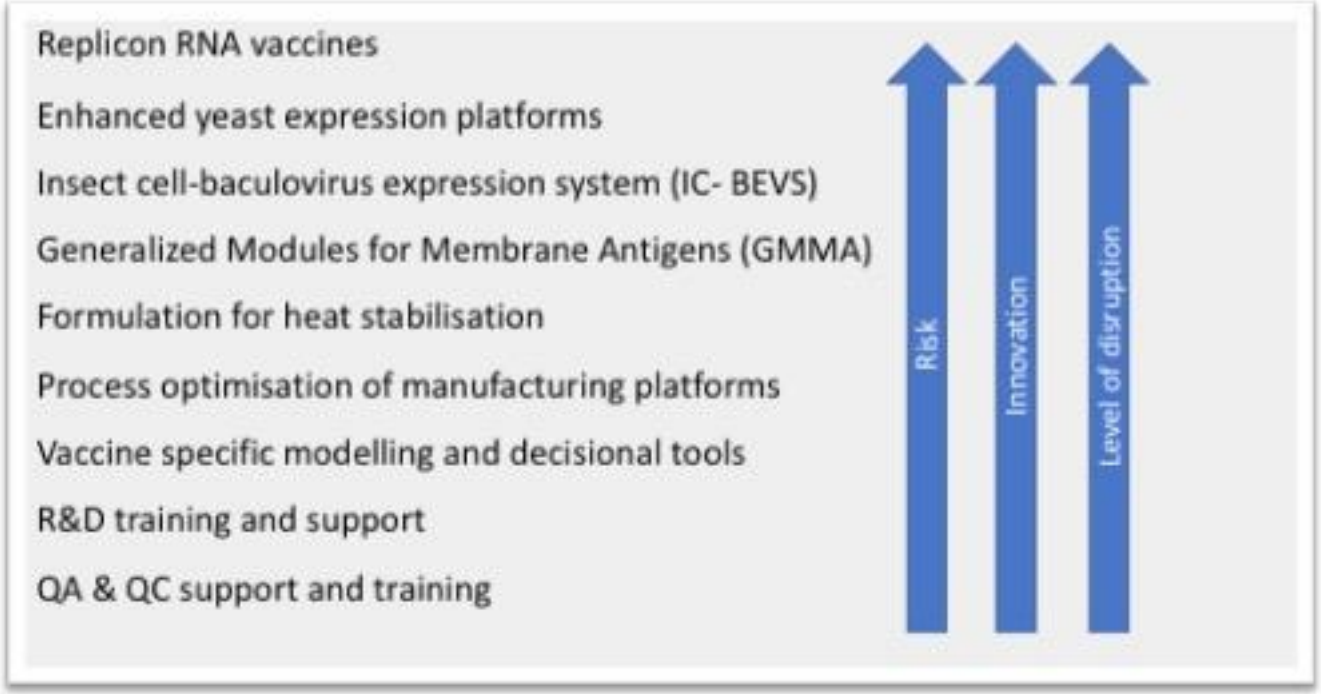


1. Provision of QA/QC support and training

- Development of QA assays for novel manufacturing platforms
- Provision of vaccine potency assays for viral and bacterial vaccines
- Development of validated assays and reference materials for emerging infections
- Advice on manufacturing QA and regulatory approval underpinning prequalification

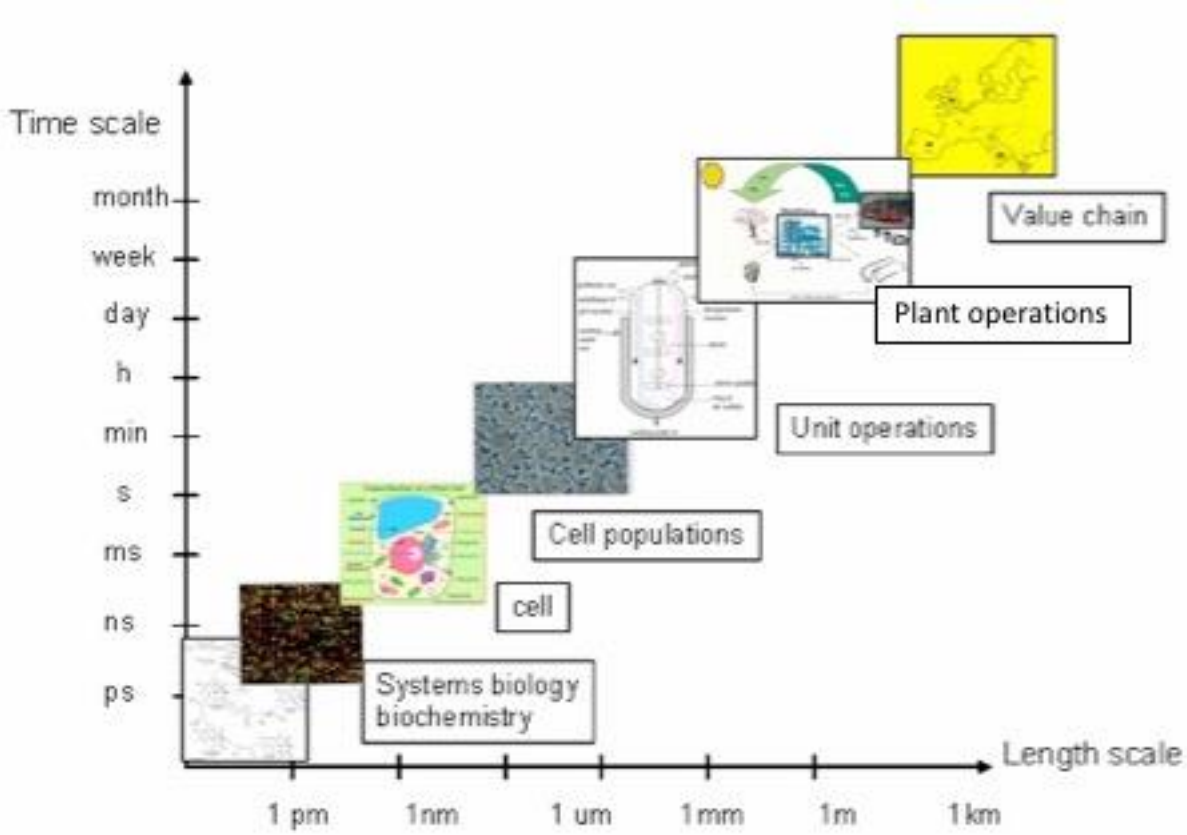
NIBSC
Confidence in Biological Medicines

National Institute for Biological Standards and Controls

2. Provision of vaccine specific modelling and decisional tools

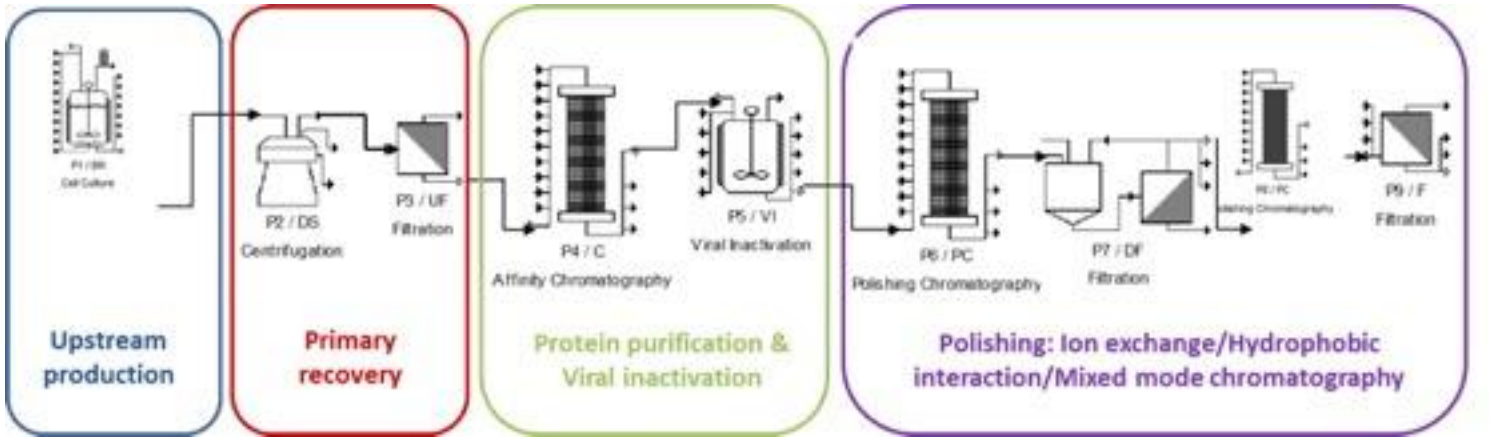
- Objectives:
  - operational efficiency for cost reduction
  - rapid response of existing assets
  - end-to-end system design
- Whole process analysis and optimisation to address bottlenecks
  - In Life Sciences: host cell system or vector optimisation for improved productivity/quality
  - In Engineering: downstream separations, formulation and packaging
  - Established computational platform for modelling and optimising vaccine manufacturing processes to reduce costs

Multi-scale modelling capabilities



Current capabilities within the hub

- We have established a computational platform for modelling and optimising vaccine manufacturing processes to reduce costs
- Apply whole process optimisation, system design and process intensification to improve operational flexibility and efficiency
- Process intensification has great promise for cost reduction and improvement of responsiveness in vaccine manufacturing
- Optimise using process mapping, bottleneck identification and process intensification, building on work in biologics manufacturing .
- Deliverable: Demonstration of benefits of integrated approach on primary production systems

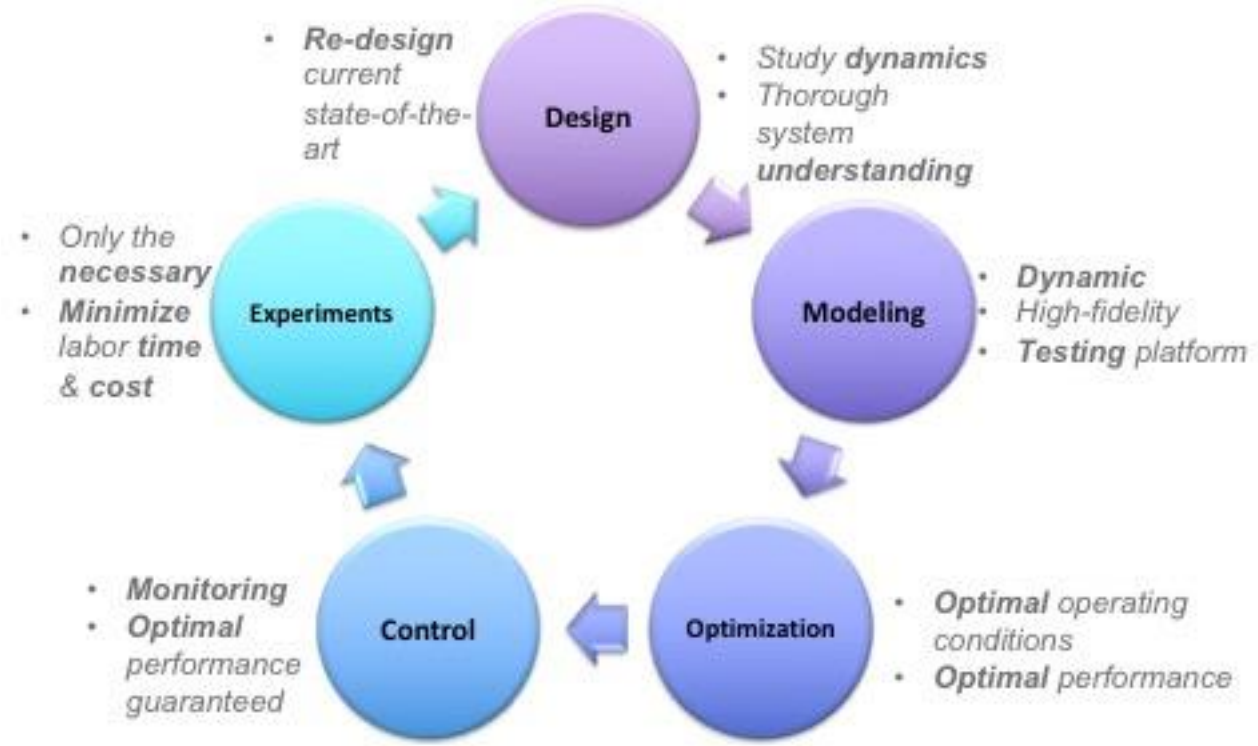


Downstream separations typically incur significant costs and in-process times

Exemplar purification concepts

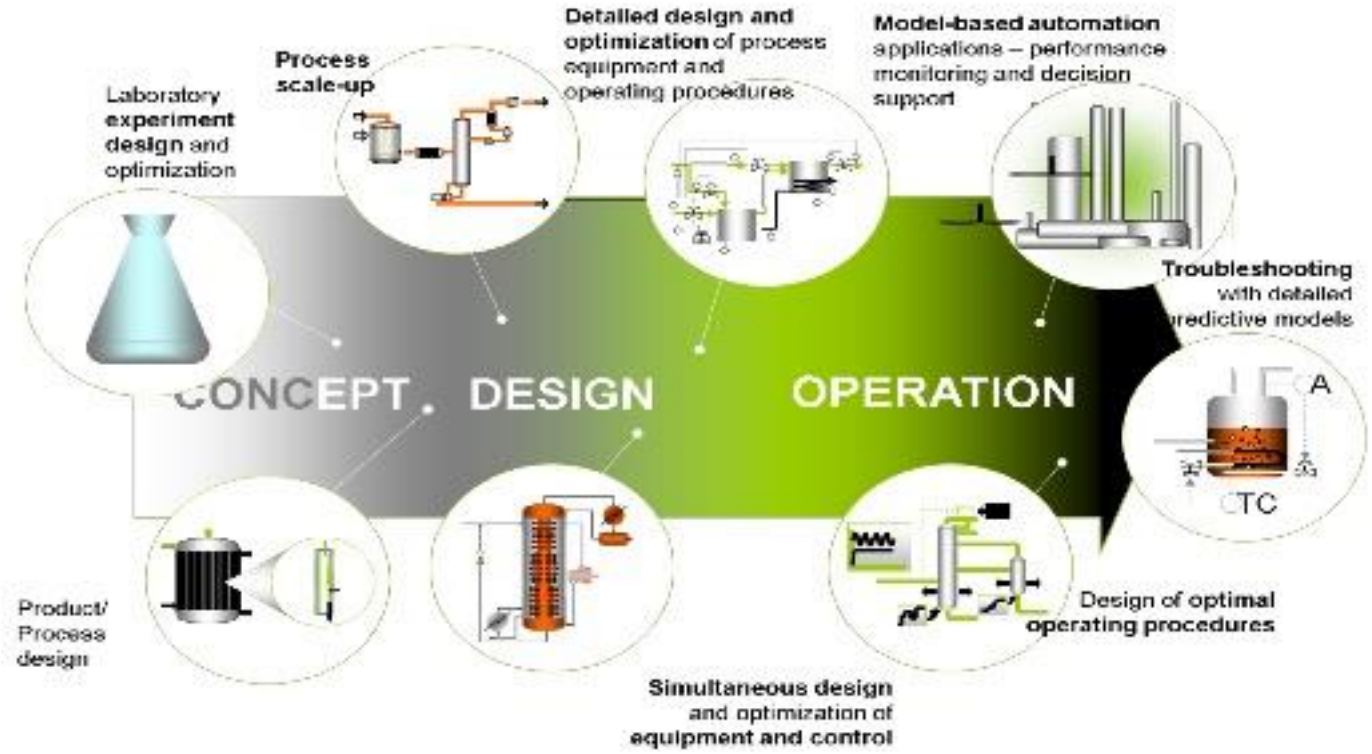
- "process telescoping" whereby several unit operations are combined into one (e.g. expanded bed affinity adsorption combining solids removal, capture and primary purification)
- continuous operation (e.g. moving to continuous chromatography using simulated moving bed technology).

- Our key activities will involve high throughput experiments, models and big data analytics.
- Deliverable: Demonstration of new vaccine separation design concepts at lab scale

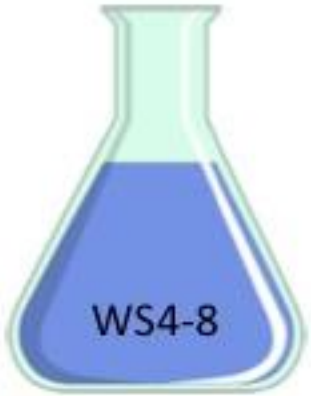


Computational models for whole systems analysis

- Multi-scale modelling of biological processes through to unit operation and whole value chains will be used for system analysis, design and manufacturing operation optimisation
- How do parameters characterising single unit performance e.g. titre, purity, recovery, formulation recipe influence whole system metrics e.g. cost per dose, lead times?



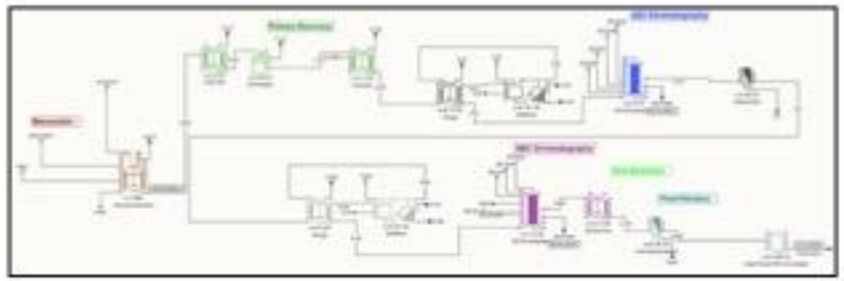
3. Process optimisation of emerging manufacturing platforms: Industrialisation, demonstration, deployment



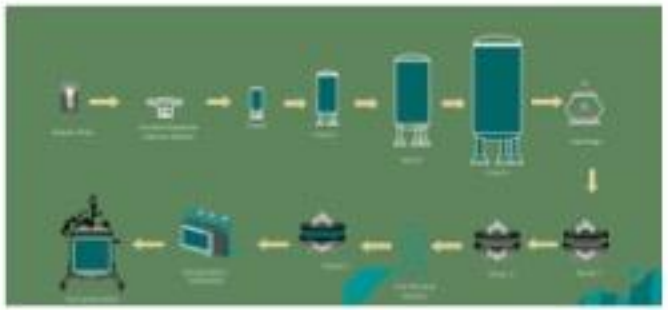
Process concepts

Manufacturing
Engineering
Design
Optimisation

10 platform designs ("blueprints")



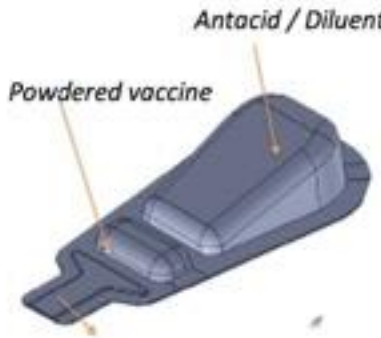
6 physical demonstrators at LMIC sites



Scale up and industrialisation analysis;
Value chain modelling and economic analysis, decision making tools
Builds on existing experience in optimising industrial processes

4. Formulation for heat stabilisation

- Advanced freeze-drying formulations and processes for vaccine stabilisation ≥ 6 months
- Generation of highly thermally-stable liquid vaccine formulations
  - (biocompatible ionic liquids, 40 °C for 12 months)
- Novel vaccine delivery formulations providing dose sparing and enhanced immunogenicity
- Wider exploitation of disposable pouch system for oral vaccine delivery



Centralised versus decentralised manufacture

Single manufacturing plant

Economies of scale and volume
Hundreds of millions of doses
Standardised QC/QA
Applicable to complex manufacture (pneumococcal conjugate vaccine)
Global distribution
High up front capital costs
High personnel costs
Low flexibility

A toolbox of technologies, training, methodologies, and material designed to meet common needs among emerging vaccine manufacturers

Central Hub

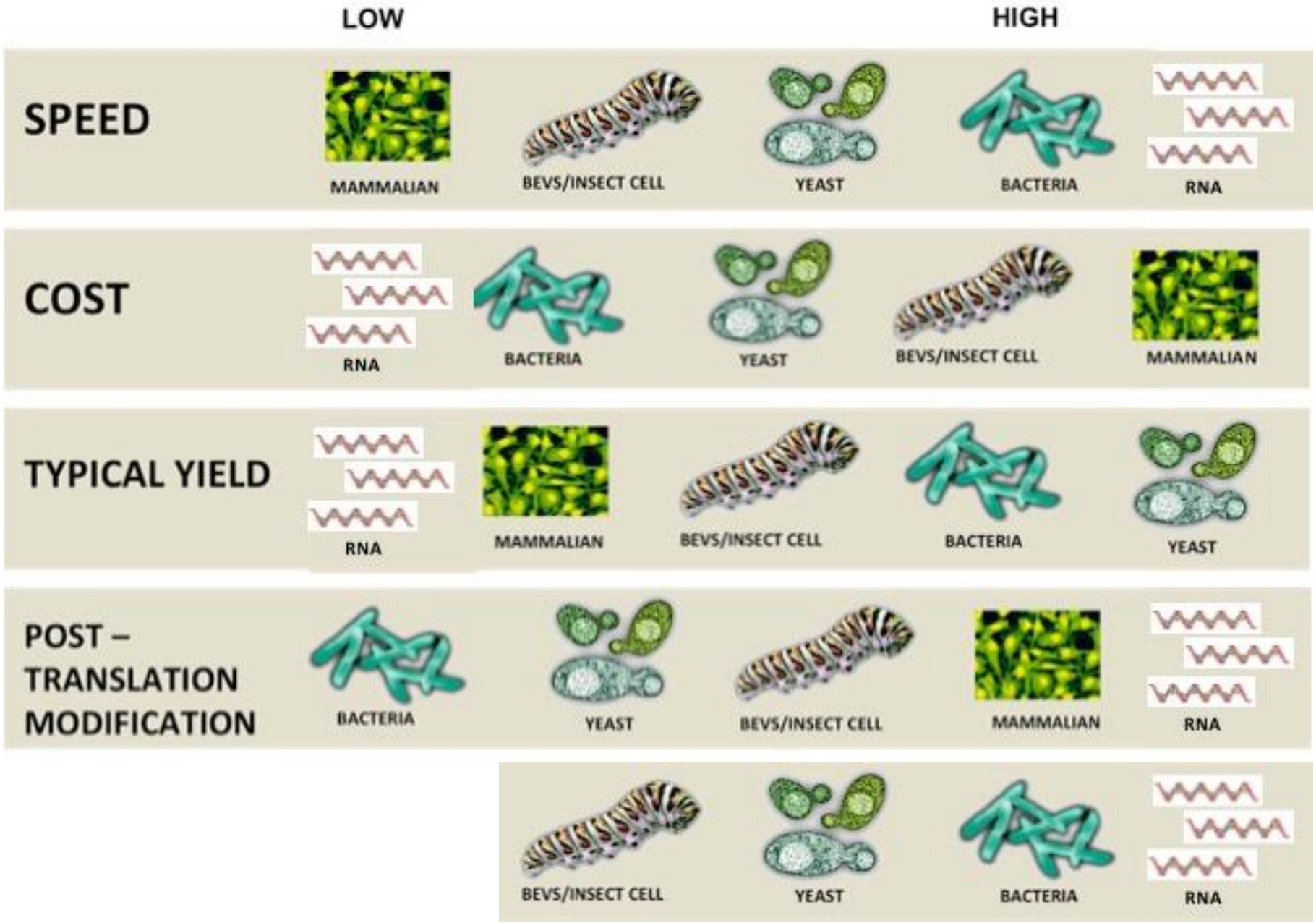
Up to millions of doses
National/regional
Neglected diseases
Rapid response to emerging and local infections
High flexibility

Staff/training
QMS
Equipment
Consumables
QA/QC testing

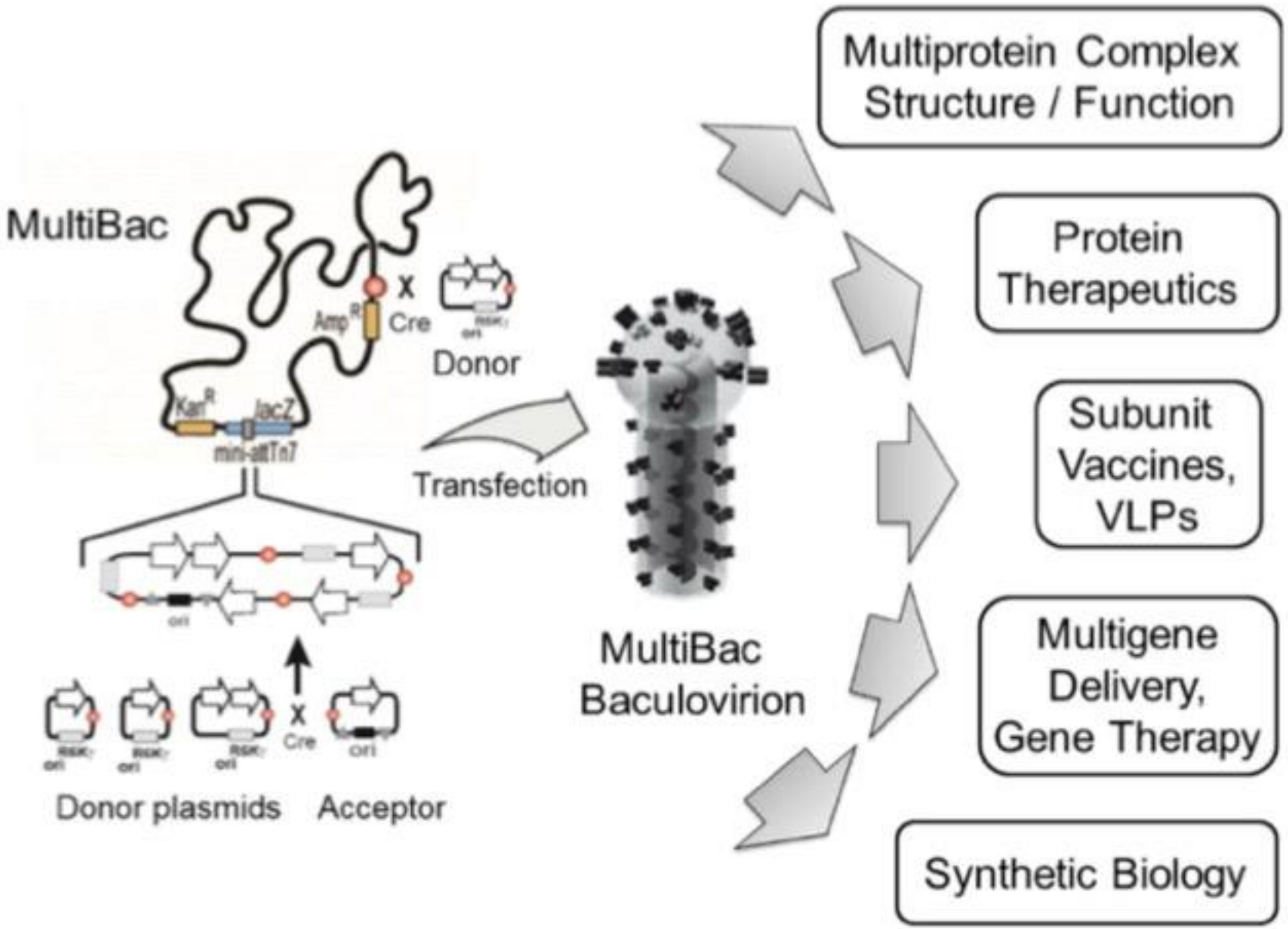
Seed technology to regional LMIC facilities capable of cGMP, fill/finish labelling

Enhanced delivery: formulation, route, supply chain…

Identifying core platforms for further exploitation

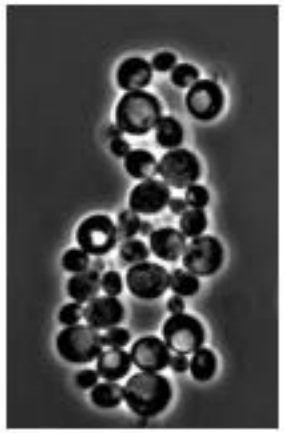


Exploitation of the multiBac Platform

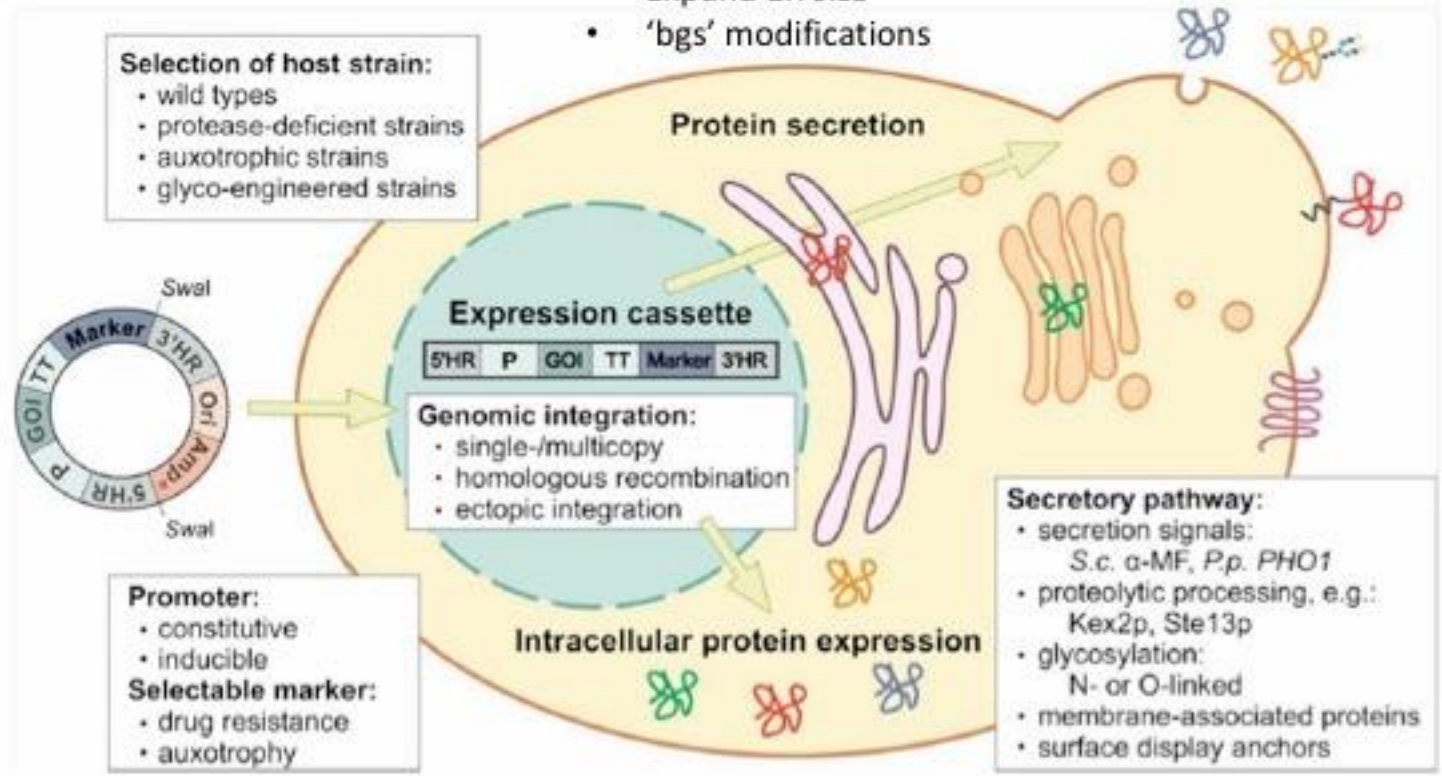


Baculovirus expression vector system (BEVS)

Engineering enhanced yeast based expression platforms



Secretory Pathway Engineering:
- Upregulate UPR
- Expand ER size
- 'bgs' modifications



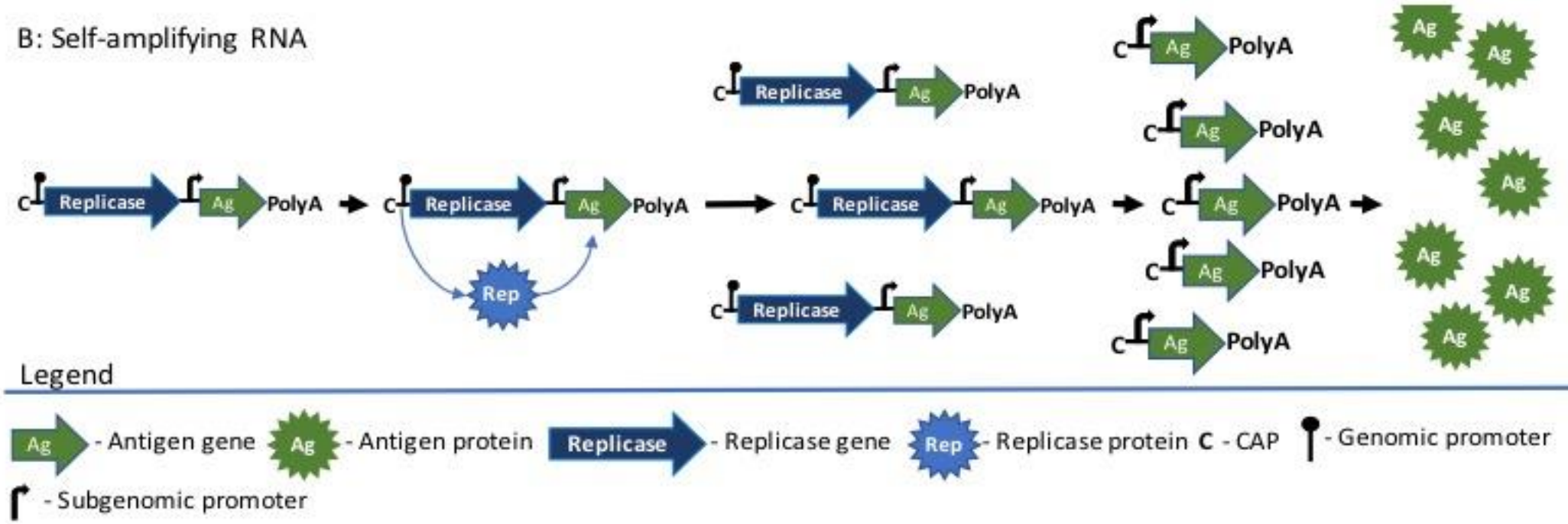
Industrial fermentation

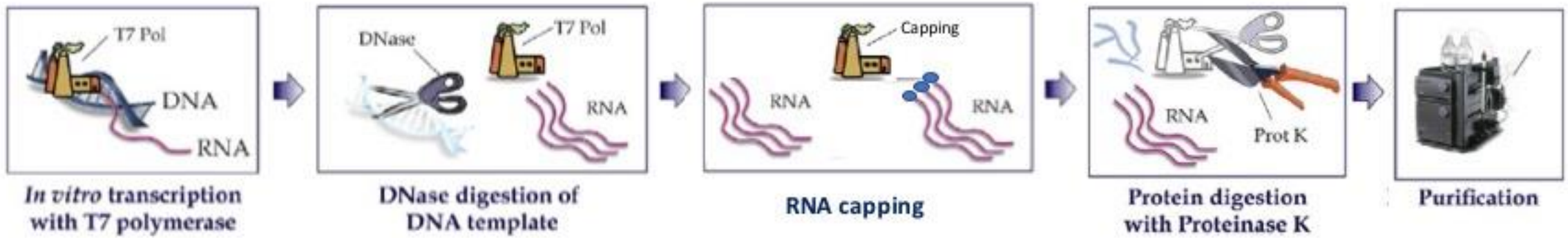
A number of individual strain modifications have been identified

We aim to combine these to create a "super-strain" and re-engineer human glycosylation

Ensure bioprocess optimisation

Self-amplifying RNA based vaccines





Fully synthetic, small foot-print, low-cost rapid manufacture

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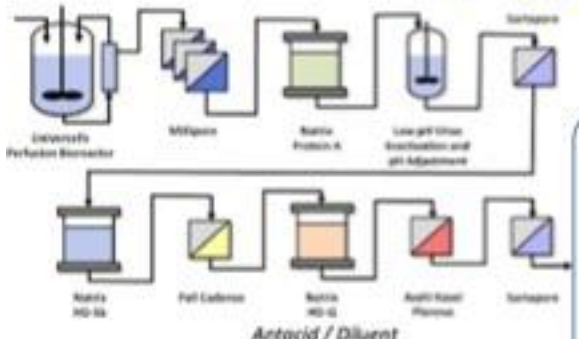
Current LMIC partnerships

- Hilleman Laboratories, India
  - development of a thermostable combined oral Cholera-ETEC vaccine
- Dalian Hissen, China
  - development of robust, modular and intensified manufacturing process capable of enhancing and accelerating yeast based production
- Incepta Pharmaceuticals, Bangladesh
  - production of formulated pilot vaccines using novel therostable stable formulations and demonstration of thermal stability and therefore the lifetime of the formulation
- Vabiotech, Vietnam
  - Establishment of a modular platform for IC-BEVS production in Vietnam
- UVRI, Uganda
  - Establishment of a modular platform for RNA production in Uganda

Future Vaccine Manufacturing Hub

Process innovation



Delivery

Advanced Technology Hub

- NIBSC
- CPI, Darlington
- NHSBT CBC, Bristol

- GSK (Global Health)
- Dalian Hissen, China
- Incepta Pharmaceuticals, Bangladesh
- Vabiotech, Vietnam

Know-how
Shared IP
Innovators

Technical
Advisors
QA/QC

Imperial College London

Formulators

Modellers
Developers

- Hilleman Laboratories – India
- UVRI, Uganda

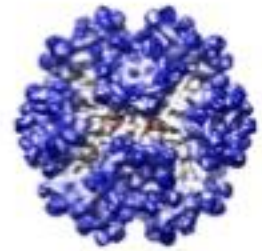
- Cambridge
- Nottingham
- Bristol
- Cranfield

Manufacturers

Manufacturers

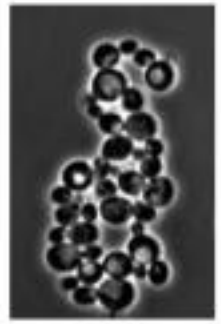
Manufacturers

Developing Countries Vaccine Manufacturers Network



VLPs

RNA



Yeast

IC-BEVS

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Opportunities for interactions & partnerships

- QA & QC support and training
- R&D training and support
- Access to Vaccine specific modelling and decisional tools
- Collaboration on process optimisation of manufacturing platforms
- Partnerships on formulation for heat stabilisation
- Partnerships on vaccine platform development
- Leveraging of existing investment to attract additional funding

Proposals

- *LMIC R&D and technology transfer flexible fund (£400,000)*
- Vaccine Hub to present, together with members at the pre-meeting symposium
- DCVMN likely to serve as platform for small grants (applications/management /reporting)
- Will provide consulting expertise for members to advance with GMP, process optimization, regulatory dossiers, PQ, investments, and partnerships with the Hub

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Thank you for your attention

Contact: r.shattock@ic.ac.uk