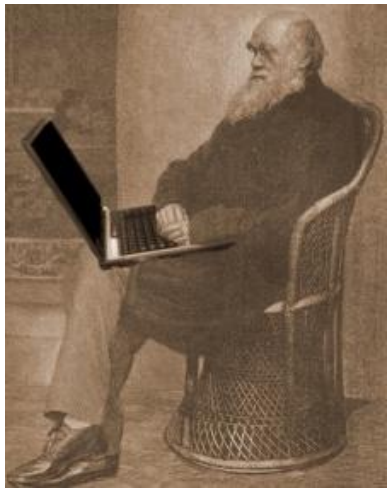


# The HPA Culture Collections

**David Lewis**
**Head of HPA Culture Collections**

# Content

- How 4 separate culture collections are integrated into a single business.
- How this business integrates with a major national healthcare agency
- How the 2 components work together to deliver health outcomes.

# The Health Protection Agency
## in the United Kingdom

An independent government organisation set up in 2003 to protect the public from threats to their health from infectious diseases and environmental hazards.

# The Health Protection Agency

## in the United Kingdom

**Centre for Emergency Preparedness and Response**

**Centre for Infections**

**Centre for Radiation, Chemical and Environmental Hazards**

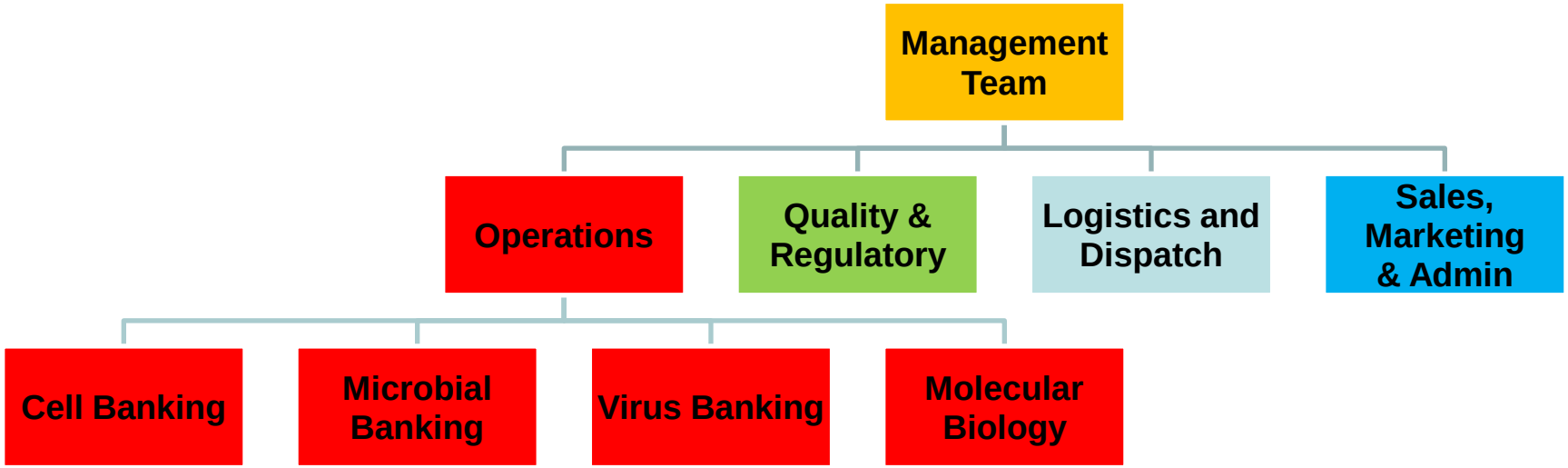
**National Institute for Biological Standards and Controls**

**Local and Regional Services**

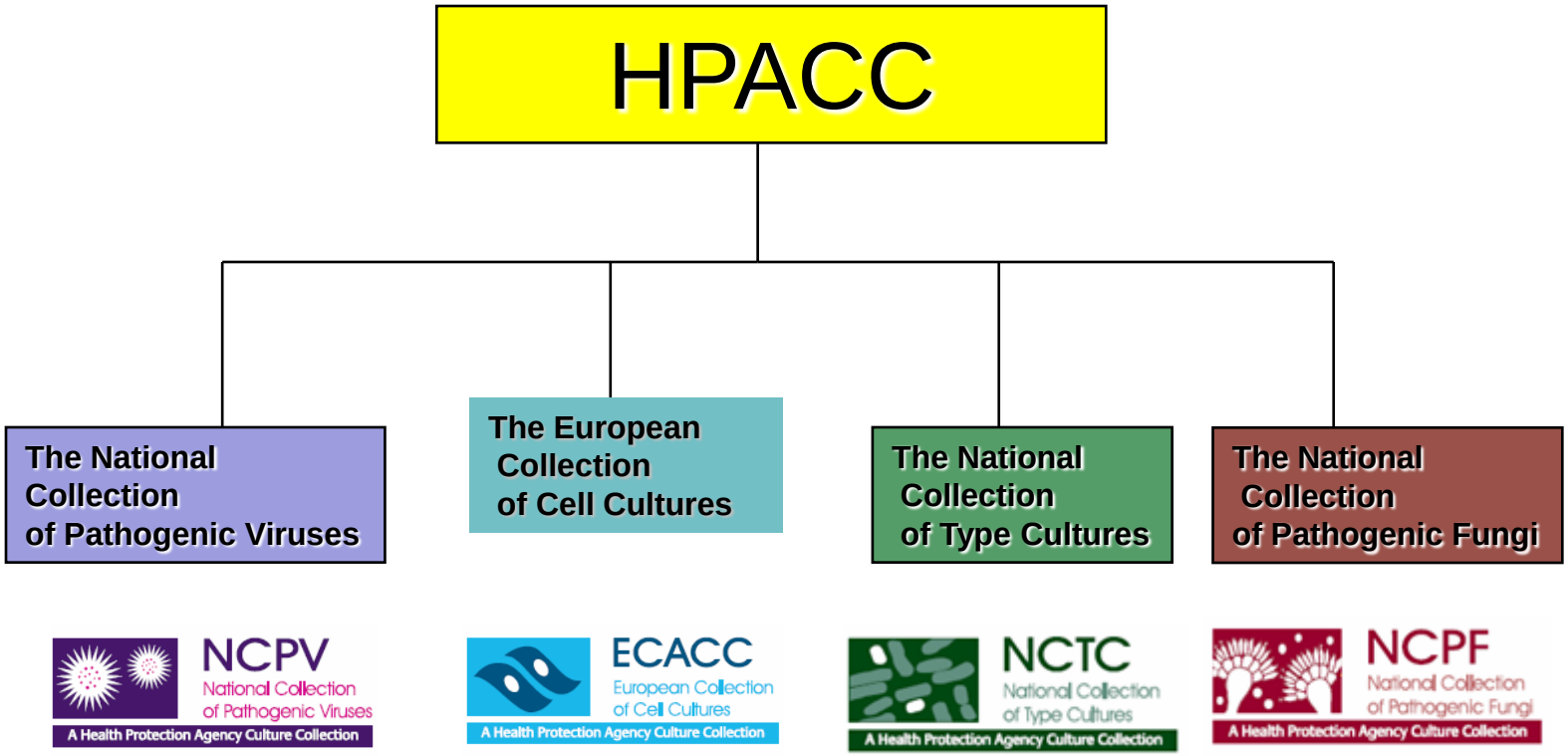
# The HPA Culture Collections

- A strategic business unit
- 90% of income from commercial sales
- Not for profit
- Research use only
- Organised as a manufacturing and marketing business.

# HPACC Organisation



# The HPA Culture Collections



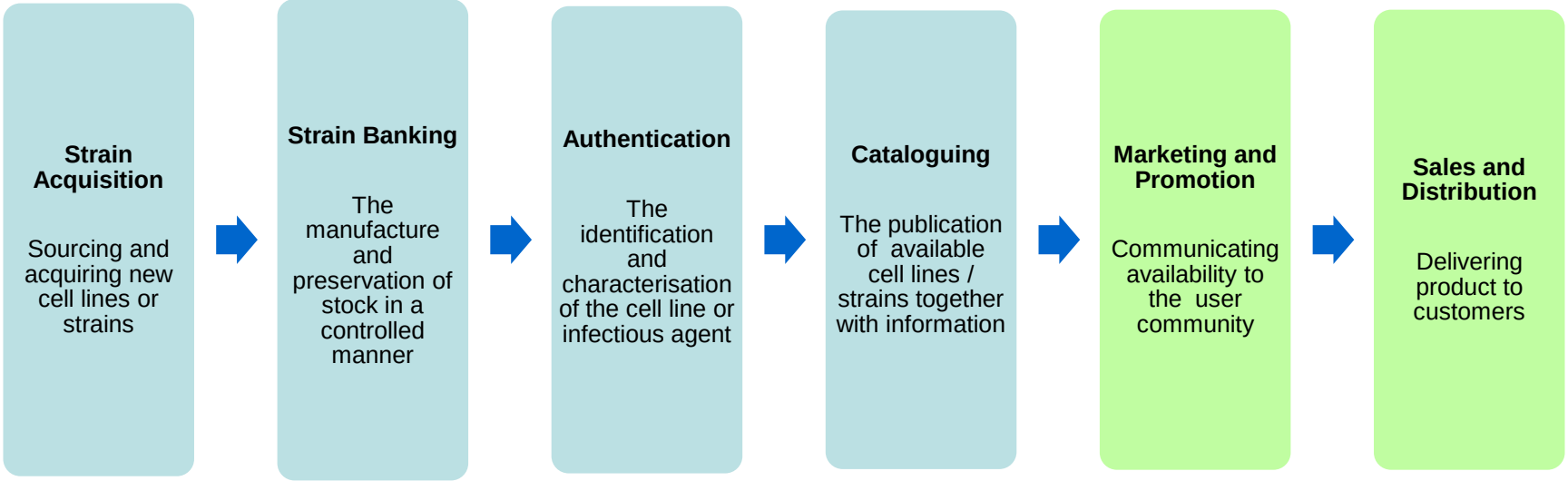
# Role of the HPA Culture Collections (HPACC)

**The supply of reference material, authenticated cell lines and human pathogens to assure the quality of laboratory health science.**

# The Fundamental Activities of a Biological Resource Centre

- Collection of strains: Acquisition
- Expand, stabilise and store: Banking
- Identify and characterise: Authentication
- Catalogue and publish: Marketing
- Supply: Distribution
- Endure: Sustainability

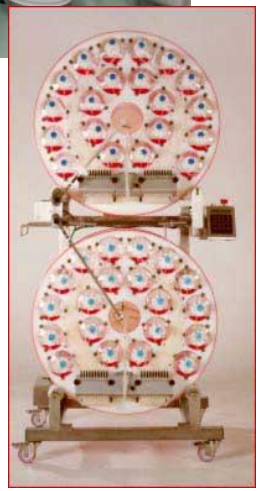
# Culture Collections Process Flow

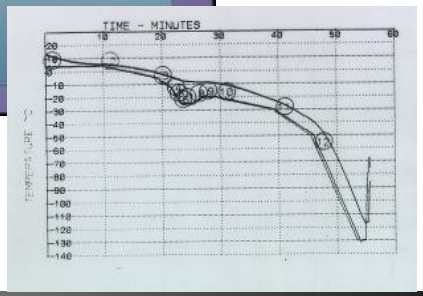


# Cell Line / Strain Acquisition

| Consideration | Cell Lines | Microbial Pathogens | Virus Pathogens |
|---|---|---|---|
| **Source** | Research product | Clinical isolate | Clinical isolate |
| **Clear Ownership** | Yes | No | No |
| **License required** | Yes | No | No |
| **Intellectual Property** | Yes | No | No |
| **Ethical** | Human donor consent | No | No |
| **Regulatory** | Human tissue legislation | Biosecurity, Biosafety | Biosecurity, Biosafety |

# Banking & Preservation



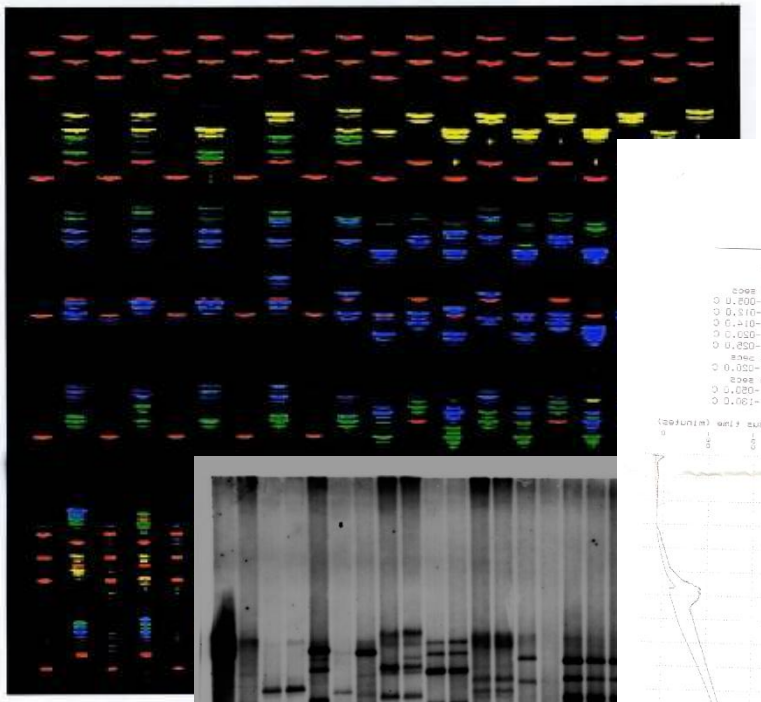
# Banking & Preservation: Common Aims

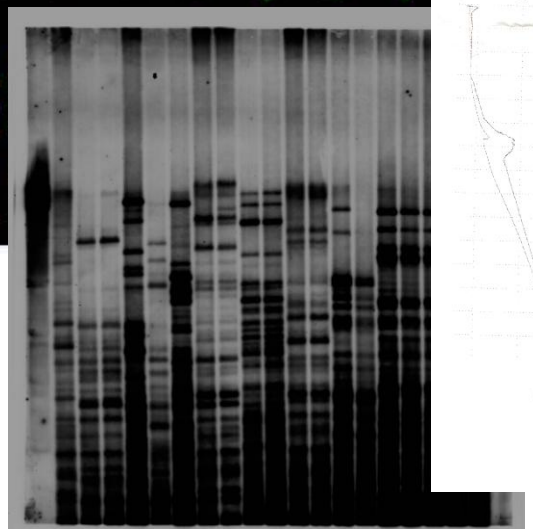
- To ensure reproducibility of the original deposit by:
  - Preserving the genotype and phenotype.
  - Building stock while minimising the time in culture.
  - Manufacturing homogeneous banks.

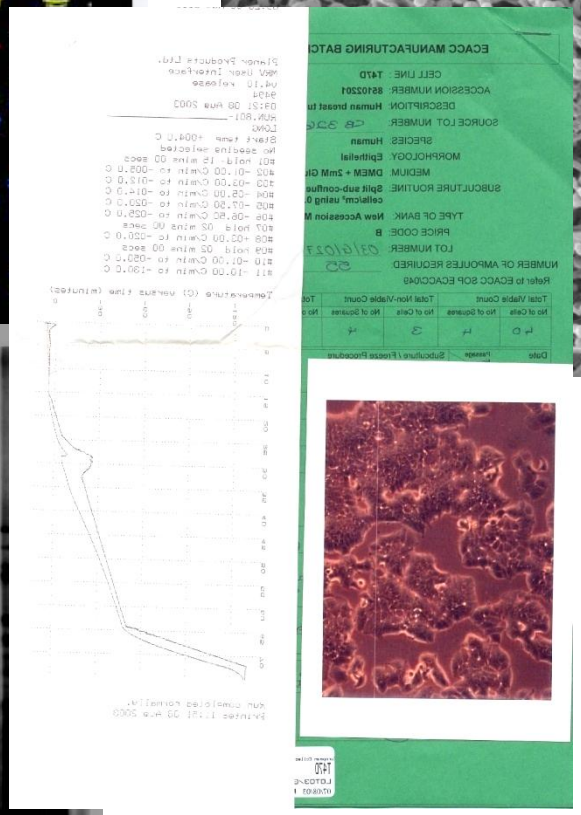
# Banking & Preservation: Variables

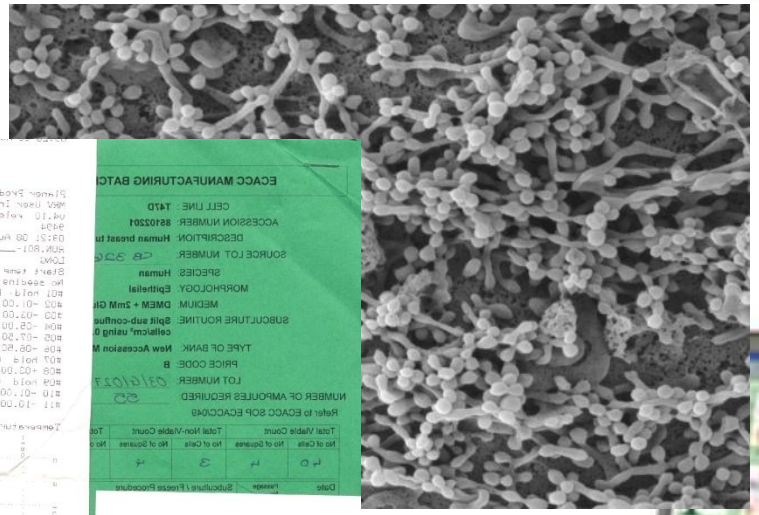
| Consideration | Cell Lines | Microbial Pathogens | Virus Pathogens |
|---|---|---|---|
| **Cultivation complexity** | Medium | Low | High |
| **Biocontainment** | BCL 2 | BCL 2-3 | BCL 2-3 |
| **Scaleability** | Medium | High | Low |
| **Purity** | High | High | Variable |
| **Preservation** | Liquid Nitrogen | Freeze-dried | -80º C / Liquid Nitrogen / Freeze-dried |

# Characterisation & Authentication



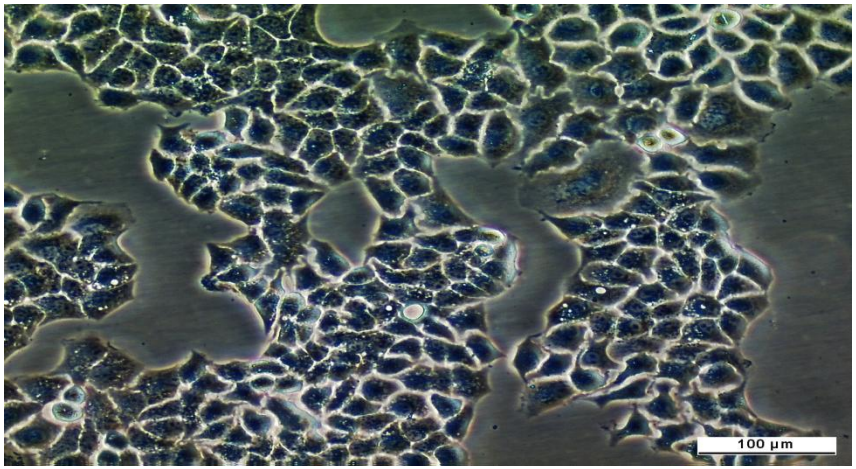


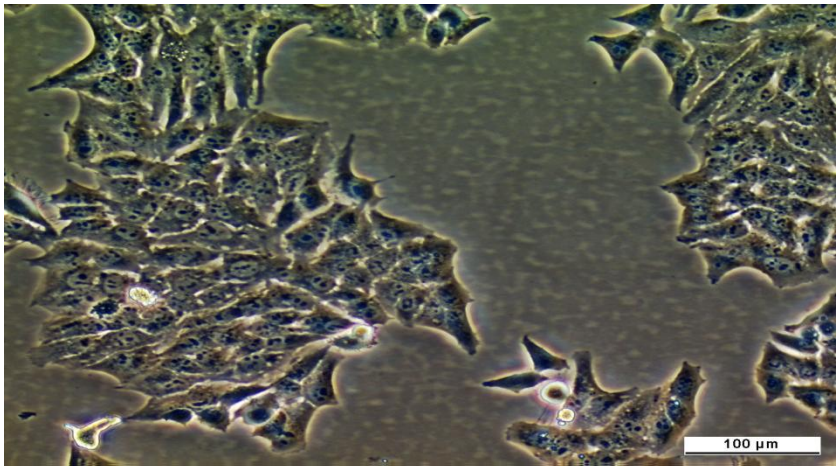


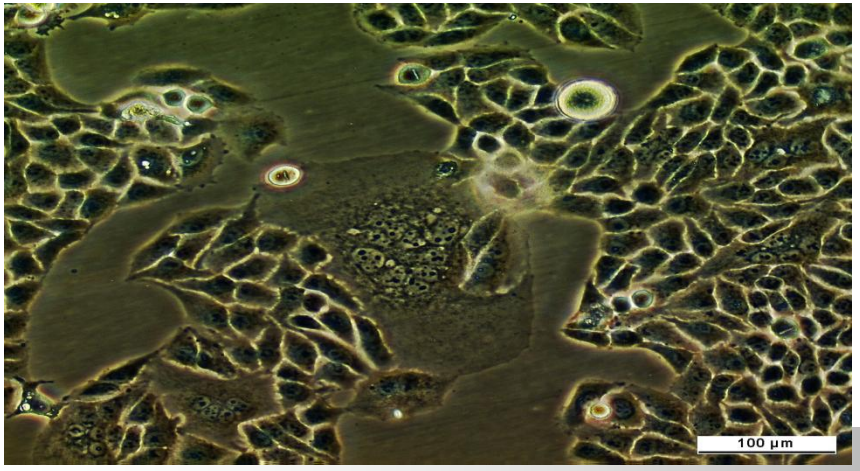


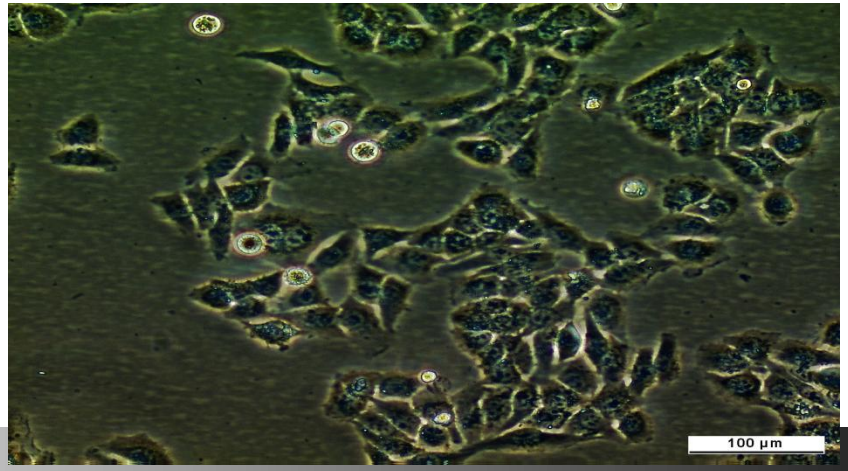
# SPOT THE DIFFERENCE.

Clockwise: Human Amnion; Human Larynx; Human Submandibular Gland; Human Embryonic Intestine.

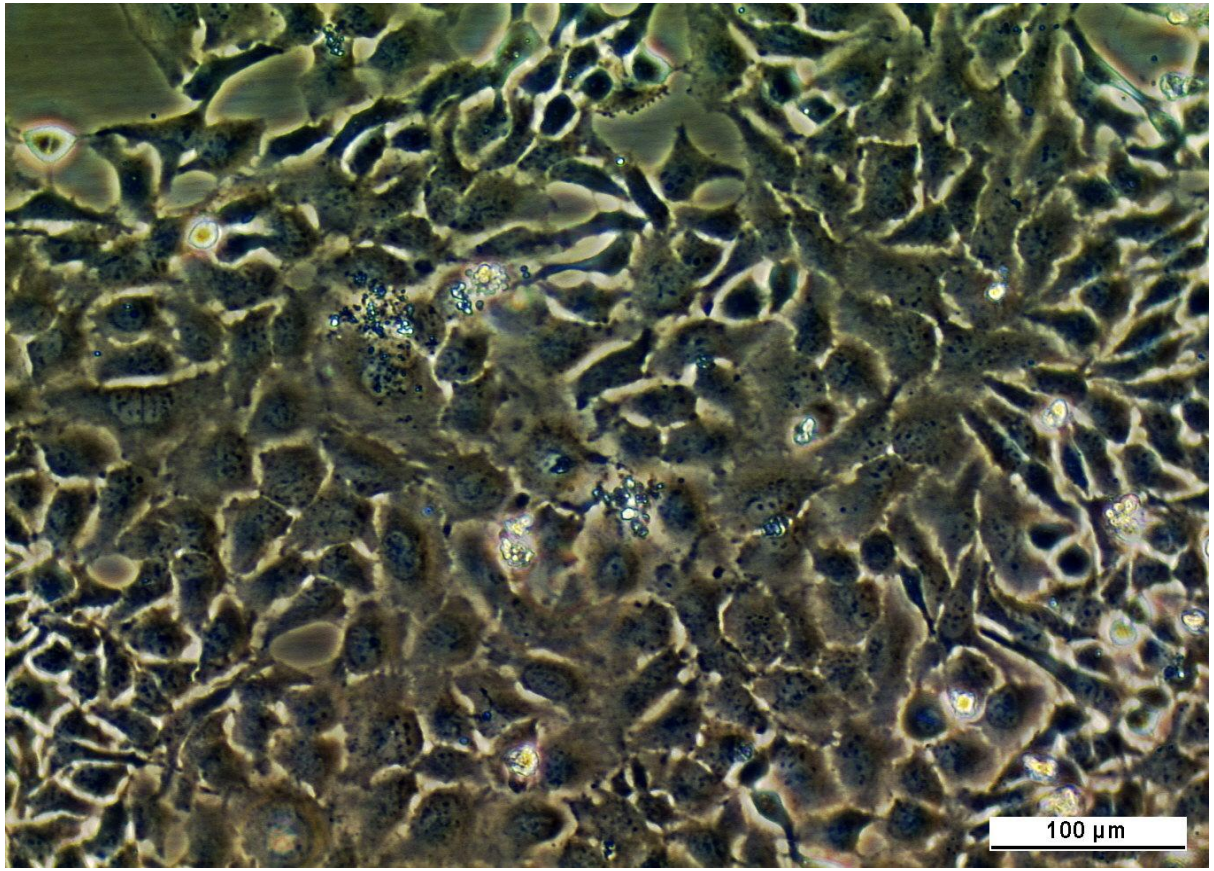


# HeLa



# Wrongly Identified Cell Lines

| *Cell line* | *Species* | *Cell type* | *Contaminant* | *Species* | *Cell type* | *Source of Data* |
|---|---|---|---|---|---|---|
| 207 | Human | pre-B leukemia | REH | Human | pre-B leukemia | DSMZ |
| 2474/90 | Human | gastric carcinoma | HT-29 | Human | Colorectal carcinoma | DSMZ |
| 2957/90 | Human | gastric carcinoma | HT-29 | Human | Colorectal carcinoma | DSMZ |
| 3051/80 | Human | gastric carcinoma | HT-29 | Human | Colorectal carcinoma | DSMZ |
| ADLC-5M2 | Human | lung carcinoma | HELA /-S3 | Human | Cervical adenocarcinoma | DSMZ |
| AV3 | Human | amnion | HeLa | Human | Cervical adenocarcinoma | ATCC; ECACC |
| BCC-1/KMC | Human | basal cell carcinoma | HELA /-S3 | Human | Cervical adenocarcinoma | DSMZ |
| BM-1604 | Human | prostate carcinoma | DU-145 | Human | prostate carcinoma | DSMZ |
| C16 | Human | fetal lung fibroblast (MRC-5 clone) | HeLa | Human | Cervical adenocarcinoma | ECACC |
| CHANG liver | Human | Embryonic liver epithelium | HeLa | Human | Cervical adenocarcinoma | ATCC; ECACC; JCRB |
| Clone 1-5c-4 | Human | Chang conjunctiva | HeLa | Human | Cervical adenocarcinoma | ECACC |
| COLO-818 | Human | melanoma | COLO-800 | Human | melanoma | DSMZ |
| DAMI | Human | megakaryocytic | HEL | Human | erythroleukemia | DSMZ |
| D98/AH2 Clone 2B | Human | | HeLa | Human | Cervical adenocarcinoma | ECACC |
| ECV304 | Human | Endothelium | T24 | Human | Bladder carcinoma | ATCC; DSMZ; JRCB |
| EJ-1 | Human | bladder carcinoma | T24 | Human | Bladder carcinoma | ATCC; JCRB |
| EPLC3-2M1 | Human | lung carcinoma | HELA /-S3 | Human | Cervical adenocarcinoma | DSMZ; JCRB |
| EPLC-65 | Human | lung carcinoma | HELA /-S3 | Human | Cervical adenocarcinoma | DSMZ |
| F2-4E5 | Human | thymic epithelium | SK-HEP-1 | Human | hepatoma | DSMZ |
| F2-5B6 | Human | thymic epithelium | SK-HEP-1 | Human | hepatoma | DSMZ |
| FL | Human | amnion | HeLa | Human | Cervical adenocarcinoma | ATCC; ECACC |
| GHE | Human | astrocytoma | T-24 | Human | bladder carcinoma | DSMZ |
| Girardi Heart | Pig | Adult heart | HeLa | Human | Cervical adenocarcinoma | ATCC; ECACC |
| HAG | Human | adenomatous goitre | T-24 | Human | bladder carcinoma | DSMZ |
| HBT-3 | Human | Breast carcinoma | HeLa | Human | Cervical adenocarcinoma | Nelson-Rees (1974) |

# Misidentification and Cross-contamination.

- Becoming well recognised for cell culture
- Many published studies invalidated through use of misidentified cell lines
- Less reported for microbial and virus culture
- The dangers are theoretically no different

# Practises favouring strain corruption

- Continuous serial culture
- Multiple strains in the same laboratory
- Imperfect segregation disciplines
- No regular verification of identity
- Exchange of non-verified strains between laboratories.

# Genotype and Phenotype

| Cultured Type | Test System | |
|---|---|---|
| | **Genotype** | **Phenotype** |
| **Cells** | Identity: DNA Profiling (STR-PCR)<br>Species: DNA 'barcoding' | Morphology; Culture Characteristics; Metabolic Markers; Surface Markers; Mass Spectrometry. |
| **Microbial Pathogens** | Gene Sequencing; Fragment Analysis (fAFLP); 16S rRNA. | Culture Characteristics; Metabolic Markers; Serology; Mass Spectrometry (MALDI-TOF-MS) |
| **Viruses** | Partial / Total Gene Sequencing | (Electron Microscopy; Cytopathogenicity; Serology) |

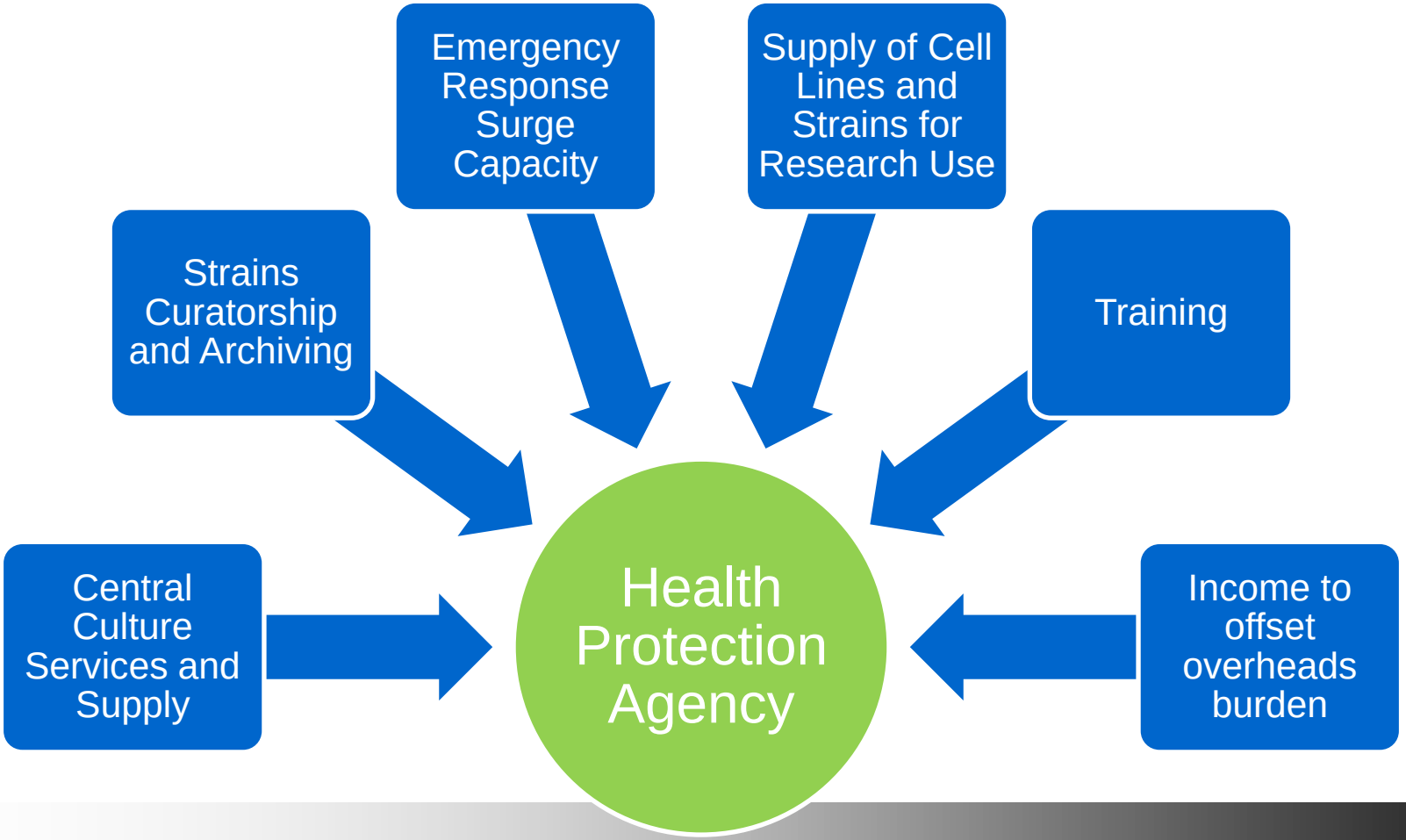
# Strain Authentication: Convergence

- Identification by gene sequencing now standard for cell lines, bacteria and viruses.
- Routine characterisation of phenotype by standard, rapid, molecular biology methods (eg transcriptomics, proteomics) becoming more feasible.

# Culture Collections:Integration with the Health Protection Agency

# Infrastructure Support

# Contribution from Culture Collections



# Benefits of a Public Sector Platform

1. Long-term stability / sustainability.
2. Enables the business to maintain primarily a national strategic role.
3. Facilitates interaction with the academic and commercial scientific communities without conflicts of interest.

# Science and Technology

- High containment (up to BCL4) facilities and expertise.
- Identification and characterisation technologies (molecular biology; gene sequencing)
- cGMP manufacturing and scale-up technologies, including down-stream processing.
- Specialist, research virology, microbiology and cell biology expertise.

# Clinical Network

- Reference Laboratories (x 21)
  - Specialist expertise in diagnosis and characterisation of particular (groups of) microorganism(eg gastrointestinal, respiratory)
- Regional Microbiology Network (x50)
  - Wide range of clinical and public health microbiology testing.
  - Includes Food Water & Environment Microbiology Laboratories. (x12)
- Local and Regional Services
  - Distributed within 26 Health Protection Units. Disease surveillance and outbreaks (incident) management.

# Fit to the Health Protection Agency

**The supply of reference material, authenticated cell lines and human pathogens to assure the quality of laboratory health science.**

# Health Science Applications of *in vitro* Culture

## Cell Culture:

- Developmental cell biology
- Cancer research
- Toxicology
- Drug discovery
- Physiology
- Diagnostic virology
- Vaccine manufacture
- Pharmaceutical manufacturing

## Microbiology:

- Clinical diagnostics
- Drug susceptibility
- Food safety
- Water safety
- Environmental monitoring
- Drug discovery
- Vaccine research
- Microbial products

# HPA Culture Collections
# Services to Health Science

- Human Clinical Genetic Research
- Cancer Research
- Drug Discovery
- Microbiology Testing Quality Assurance
- Infectious Disease Emergency Response.

# HPACC
# Human Genetic Cell Bank

- Strategic support to the Human Genome Mapping Project.
- Lymphoblastoid cell lines produced for >20,000 cases.
- Manufactured and store cell banks for most major UK epidemiological genetics studies.
- >200 Diseases represented.

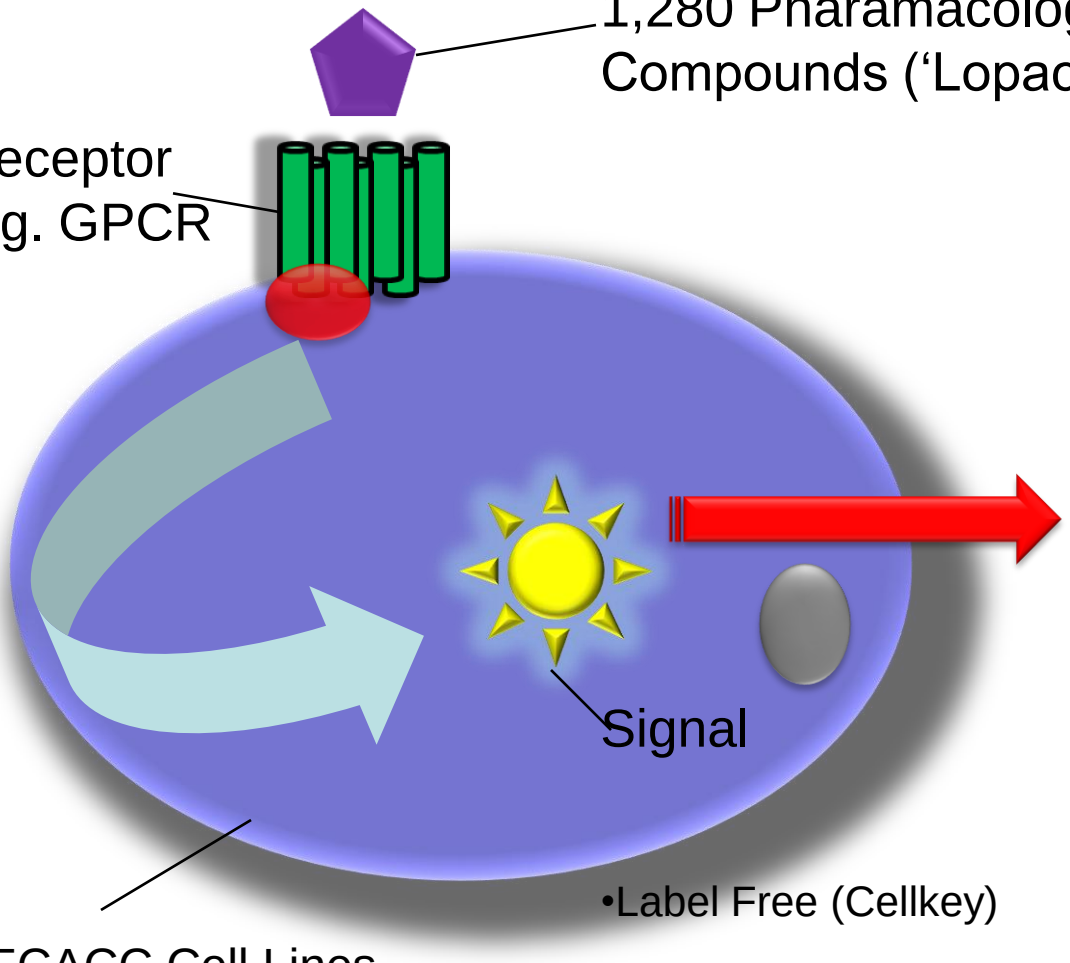
# Cancer Research

Major provider of, and repository for authenticated human tumour cell lines for cancer research.

# Drug Discovery: Cell Surface Receptor Panning

1,280 Pharamacologically Relevant Compounds ('Lopac' library)

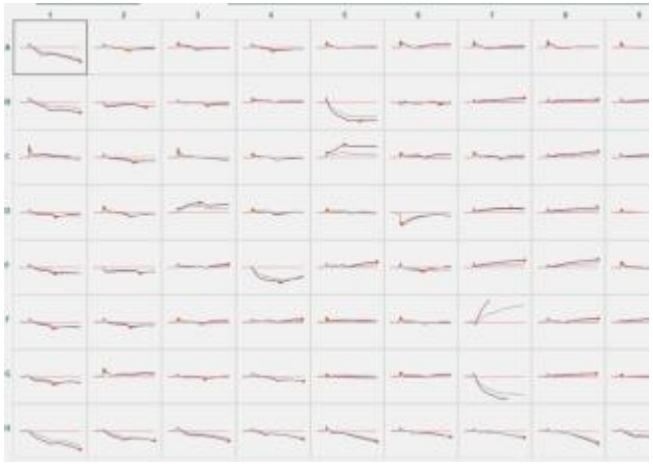
Receptor e.g. GPCR

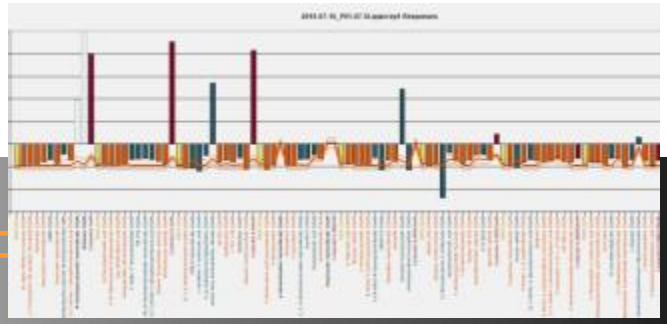


Signal

ECACC Cell Lines

Receptor "panned" profile of cell line





- Label Free (Cellkey)
- Label Dependent (FLIPR)

# Microbial Testing

**Manufacture of Quantitative Controls, e.g. NCTC LENTICULE Discs®, for Food & Water testing**

**Virus Proficiency Testing Panels for internal quality assurance schemes**

# Infectious Disease Emergency Response

**H1N1 Flu Pandemic.** The HPACC:

- Banked the outbreak strains
- Expanded the new isolates for laboratory and animal studies.
- Banked the reassortant vaccine strain
- Made staff available for diagnostic testing and epidemiological support.

# Summary

- How different culture collections have integrated as a single business
- How the business integrates with a government health agency
- How the 2 can assist each other to deliver service to health science.
- **IT WORKS QUITE WELL.**