



The Pirbright Institute



The Pirbright Institute



Inside the high-containment building



Inside the high-containment laboratories



New low-containment building

- Containment Level 2 Laboratory
- Work started in 2013
- Commissioned 2016
- Cost £100m



Our science

Research at the Institute is a synergistic combination of fundamental and applied science, based upon a wide range of expertise, and unique biological and physical resources. The science strategy is delivered through three strategic programmes:

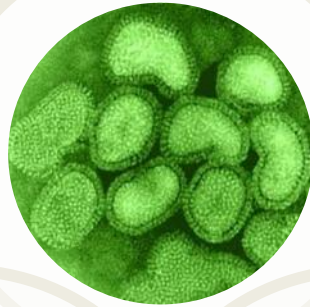
- **Avian Viral Diseases**
- **Livestock Viral Diseases**
- **Vector-borne Viral Diseases**

Each programme comprises a platform of fundamental science projects that provide the new knowledge that is then translated, within the programmes, into applied science.

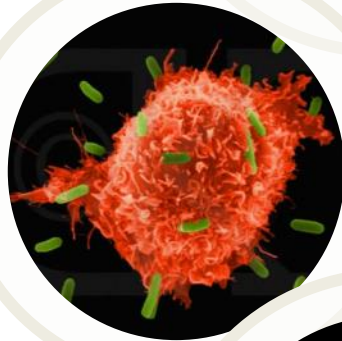


Interactions between disciplines

Diagnostics, disease surveillance, mathematical modelling



Virus biology, gene functions, evolution



Immune responses to virus infections & vaccines



Virus-host interactions in infection models in natural hosts



Role of arthropod vectors in virus transmission

Impact of foot-and-mouth disease

A FREE VIDEO FOR EVERY READER SEE PAGE 20 FOR DETAILS

THE INDEPENDENT

MONDAY 26 FEBRUARY 2001 No 4,480 ***** (R35p) 3p

RUDE BOY JOHN WALSH MEETS DAVID STARKEY REVIEW FRONT

The cull widens as the contagion grows

By MICHAEL McCORMICK, Nigel Morris and THOMAS PERRY

THE FOOT AND MOUTH disease that has brought British farming to a virtual standstill had spread right across the country yesterday and could even have reached mainland Europe, as desperate efforts to contain the virus appeared to have failed.

Despite mass slaughter of infected animals in the West Country, Britain's largest livestock region, joined Northumberland and Devon in a warning of infection, and the situation grew grimmer still when it was found that the Devon farmer concerned was a regular exporter of livestock to Europe.

Five farms and abattoirs were yesterday put on high alert by the Ministry of Agriculture, Fisheries and Food (MAFF), including the first suspected case in Wales. A sheep with the disease was traced to a farm in Northumberland, where it was found to be infected with the virus.



A giant bonfire of dead pigs and cattle in Northumberland, ordered by officials.

A spokesman for the MAFF said officials organising the overnight bonfires on a farm in Little Wymondley, Essex, said they were an extraordinary job. Some of our staff have been working 16-hour days. Earlier, the government's senior vet in the Southwest said there could now be a crisis on the scale of the last and most widespread epidemic of 1967, in which nearly 200,000 animals were slaughtered.

As MAFF officials tried yesterday to trace all rest stops where sheep and cattle were likely to have been, the government's senior vet in the Southwest said there could now be a crisis on the scale of the last and most widespread epidemic of 1967, in which nearly 200,000 animals were slaughtered.

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INSIDE: Alexander 14, Ephraim 15, Femall 24-25, Dempster 47, TV & Radio 61-64, Letters 65-66, Coffee Break 78-80, City 81-85

DEADLY VIRUS THAT HAS SHUT DOWN THE COUNTRYSIDE

THIS is the virus which has paralysed the countryside and left farmers in fear of financial meltdown. By last night, Keep Out notices had been slapped on all farmland in Britain in a desperate battle to stop the spread of foot-and-mouth.

Hunting was banned, postmen were ordered to leave deliveries at farm gates and rambles were warned to keep away from areas containing livestock. So infectious is the disease, shown here in a remarkable computerised image produced by Oxford University, that merely walking across an affected field can transfer it to neighbouring areas. It can be carried under the fingernails after contact with an infected animal. And released into the air, it can travel on the wind to strike down cows, pigs and sheep hundreds of miles away. After another case of foot-and-mouth was confirmed in Essex yesterday, there were demands for a mass cull of thousands of animals.

SEE PAGES 6 & 7

FARMERS WEEKLY

Mar 2 - Mar 8 2001 £1.50 www.fwi.co.uk

FREE INSIDE: GUIDE TO GRASSLAND NUTRITION

ARABLE ADVICE: PUTTING CROPS BACK ON TRACK FOR TOP YIELDS

TRACTOR TESTS ON TRANSMISSIONS page 90

Foot-and-mouth crisis: The tragedy unfolds

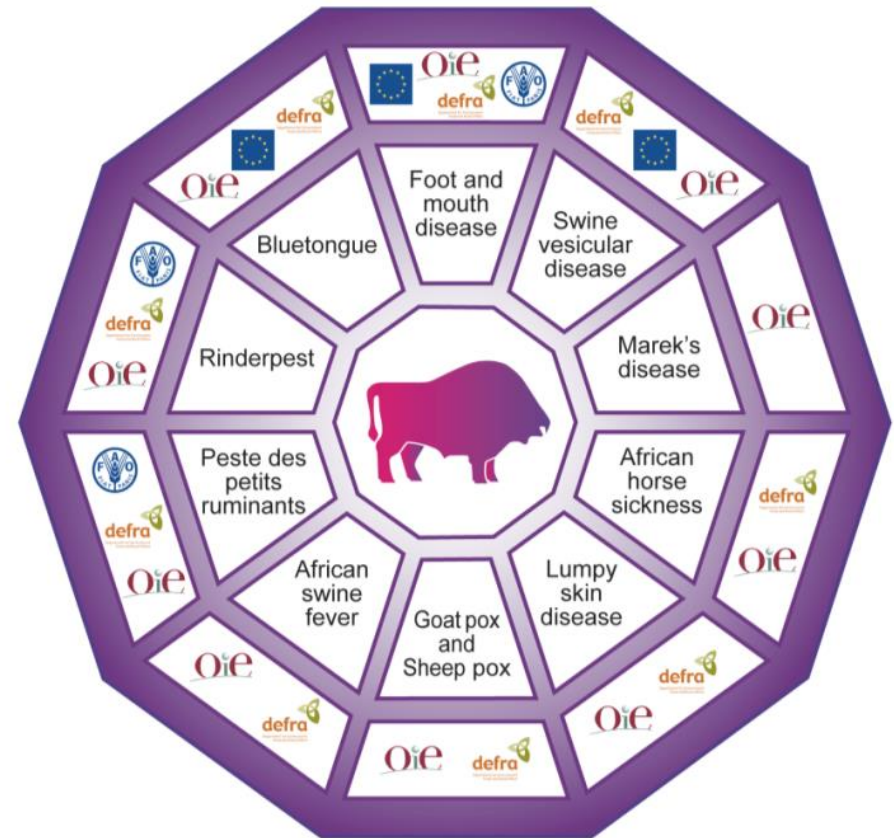
pages 6, 19, 35, 39, 106





A RED BUSINESS PUBLICATION

Annual global impact estimated at \$5 billion

BBSRC National Virology Centre: The Plowright Building

- 2015: Occupied new high containment laboratory
- Houses all our work with “live” FMD and International Reference Laboratories for FMD, BT, PPR, ASF, AHS, Capripox



	WRL = World reference laboratory of FAO
	RRL = Regional reference laboratory of OIE
	EURL = Community reference laboratory of EU
	DEFRA = UK reference laboratory

Key reference laboratory activities at Pirbright



FMD diagnostics training course – April 2013

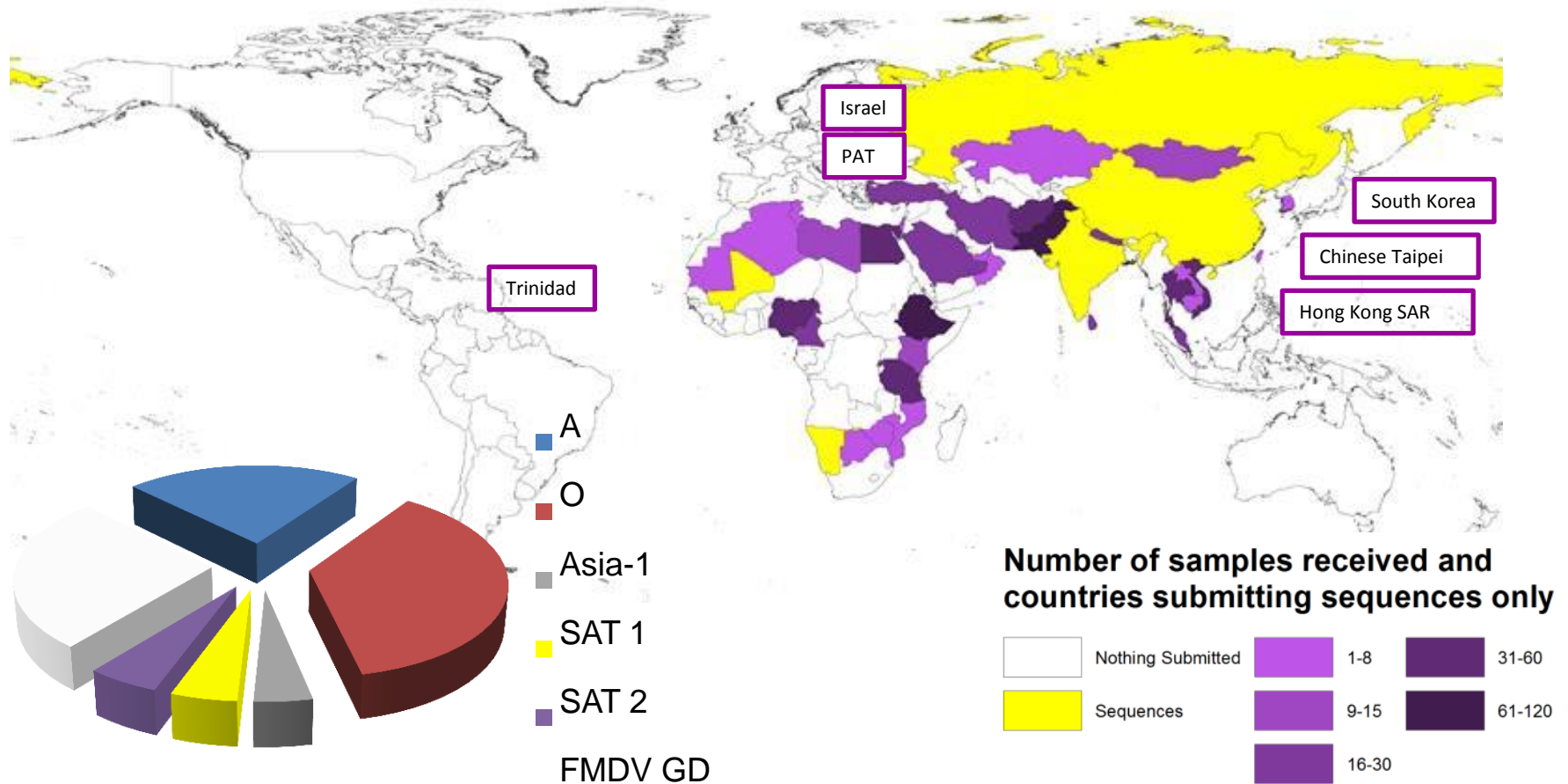


Vaccine matching training course – Sept 2013

- Contingency planning and emergency response
- Referral diagnosis, international surveillance, vaccine selection
 - 50 FMDV samples/year tested FoC
- Test harmonisation and quality control
- Training
- Virus and sample collections
- Applied research - new diagnostics and virus characterisation methods
- Links to strong research base

Submissions to WRLFMD Pirbright

October 2013 – September 2015



- Sequence exchange with China, Russia, India and BVI
- Reports for these samples can be found at: www.wrlfmd.org

Coordinating Global Networks

OIE/FAO FMD Laboratory Network



- OIE and FAO Reference Centres (+ affiliates)
- Annual meeting and report
- **Global surveillance and changing patterns in risk pathways**
- **Harmonised and improved lab capacity**

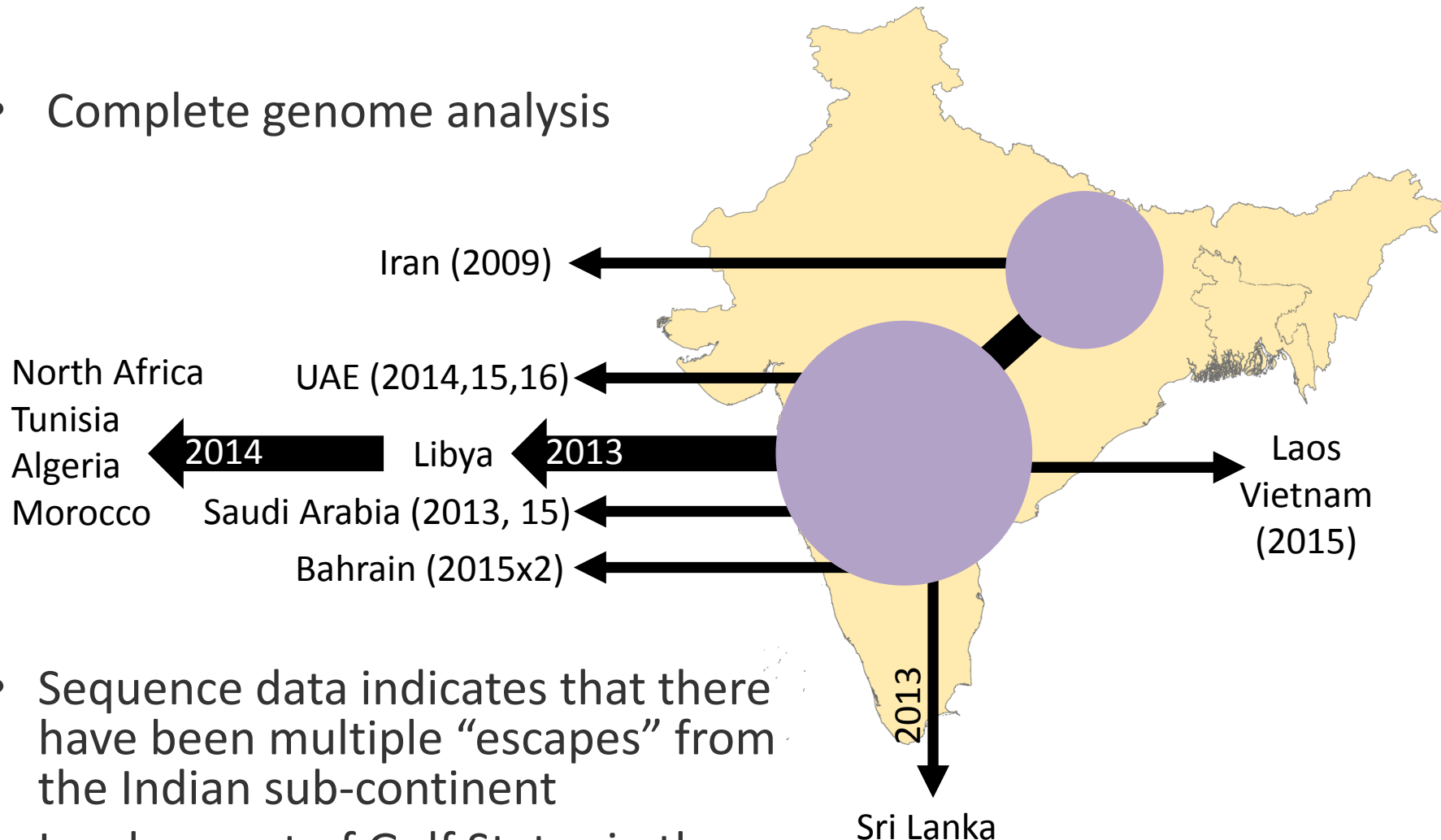


Brescia, Italy – November 2014

O/ME-SA/Ind 2001

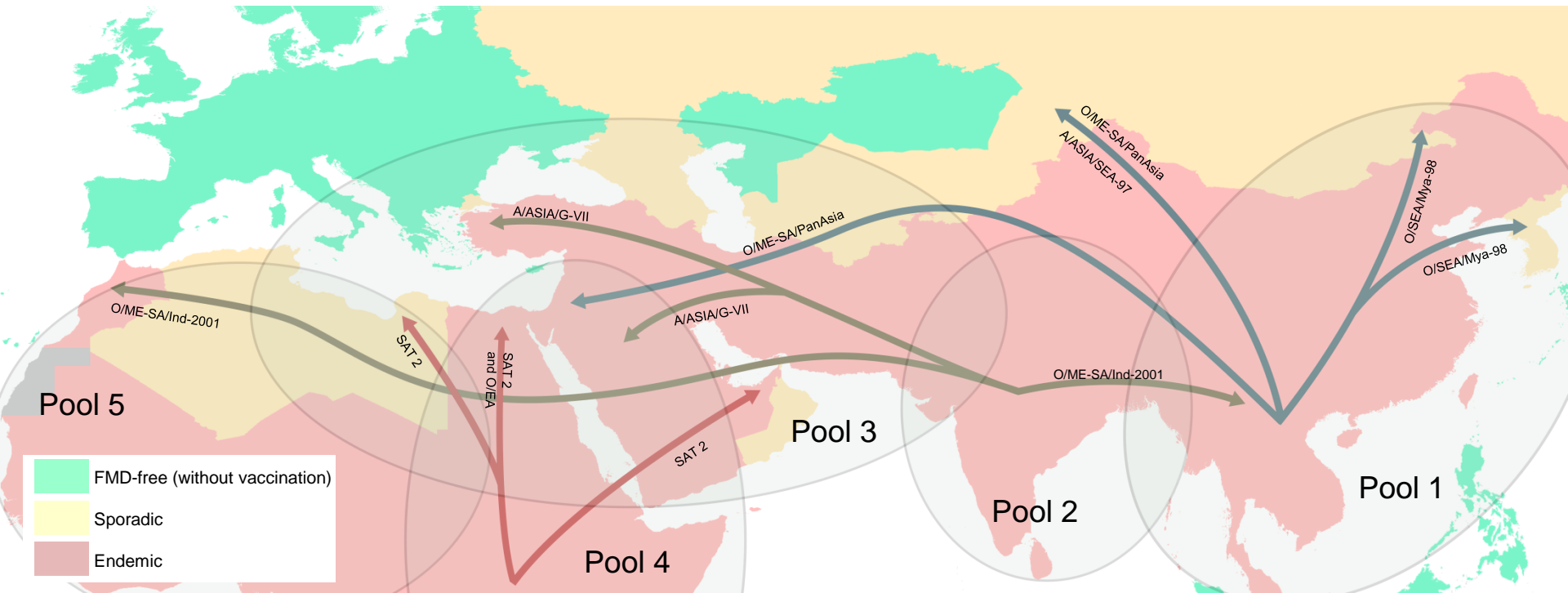
New full genome analysis

- Complete genome analysis

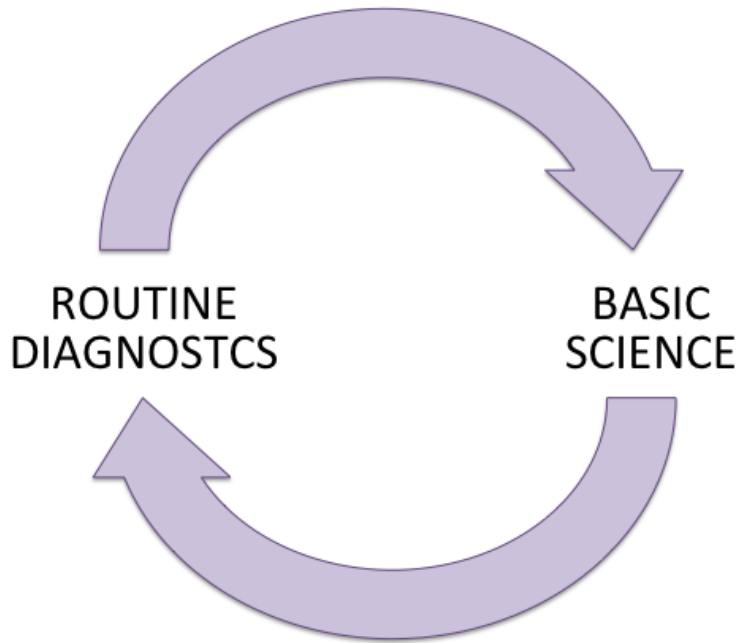


- Sequence data indicates that there have been multiple “escapes” from the Indian sub-continent
- Involvement of Gulf States in the epidemiology of these outbreaks ?

- The epidemiology of FMD in the regions is very dynamic and recent trans-boundary movements of the virus require close monitoring
 - Opportunities for collaborative work with Taiwanese Scientists



Relationship with research programmes



Reference Laboratory

- Routine testing
- Molecular epidemiology
- Emergence of new strains
- Performance of vaccines

Applied Research

- Assay development and validation
- New assay formats

Fundamental science

- Mechanics of viral evolution
- Viral replication
- Vaccine immunology
- Drivers of antigenic change

Acknowledgements

- Support for the WRLFMD and research projects
- Collaborating FMD Reference Laboratories and field teams
- Partners within the OIE/FAO FMD Lab Network



Department
for Environment
Food & Rural Affairs

www.pirbright.ac.uk

Welcome to the University of Surrey

Proud to be University of the Year – *The Times & Sunday Times Good University Guide 2016*

90% STUDENT
SATISFACTION IN
NSS

4th GUARDIAN
UNIVERSITY
GUIDE 2016 &
2017

95% AVERAGE
GRADUATE
EMPLOYABILITY
OVER 5 YEARS

A TOP
UNIVERSITY
FOR SPORT

THE  TIMES
THE SUNDAY TIMES

GOOD
UNIVERSITY
GUIDE
2016

UNIVERSITY
OF THE
YEAR

Tell us about your day: @uniofsurrey #SurreyOpenDay

Research & Teaching

WORLD

LEADING
RESEARCHERS IN
THE CLASSROOM



£400m+

INVESTMENT
TO IMPROVE
CAMPUS
FACILITIES



£45M

NEW VET SCHOOL
(1 OF 8 IN THE UK)



80%

OF STUDENTS
LEAVE WITH A
2:1 OR FIRST



89%

STUDENT
SATISFACTION
WITH TEACHING
IN NSS 2016



ONLY

UNIVERSITY WITH

3

QUEENS
ANNIVERSARY
PRIZES

5G

INNOVATION
CENTRE IN
COLLABORATION
WITH GLOBAL
TELECOMS



**LIFE-
SAVING**

WATER
QUALITY
RESEARCH



NEW

DRUG
DETECTION
TECHNOLOGY
RESEARCH



A new vet school; a fresh approach to veterinary education

Background:

UK's eighth
vet school

Second to be
opened in last
50 years

7 student
applications
for every place

International
demand for
vets in the
areas of
livestock,
research &
pathology



Timeline:

First
cohort of
48
students
2014

120
students
per year
from
2015

RCVS
Accreditation
2019

What makes us different?

Our location:
uniquely placed for our network
of practice partners, industry
and government

Campus:
encouraging collaborative pan-
university ventures

Distributed teaching model:
students feel part of the
profession from day one





State-of-the-art facilities



Conference-standard
lecture theatres

Clinical skills suite -
teaching technical and
examination skills

Mock practice consulting
rooms - communications
training

One of Europe's largest
and most sophisticated
pathology facilities

World-class Veterinary Pathology Centre



Teaching, research,
surveillance &
diagnostics
capabilities

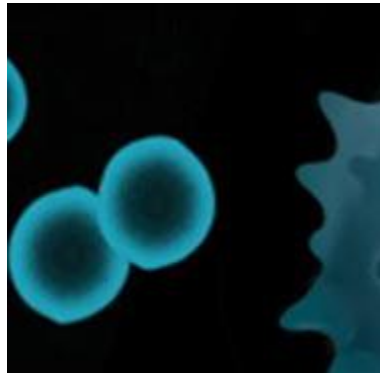
State-of-the-art
teaching rooms in
our Veterinary
Pathology Centre

A team of board-
certified
pathologists

A thriving student
pathology society

93%

of our biosciences, health and veterinary research was rated world-leading or internationally excellent in the latest UK research excellence framework (REF 2014)



Our staff publish in the top impact factor journals in their field, as well as in the very best interdisciplinary journals e.g. Nature

Extensive, well-established collaborations with industry and the NHS continue to provide knowledge transfer to the commercial sector, clinical practice and the wider community



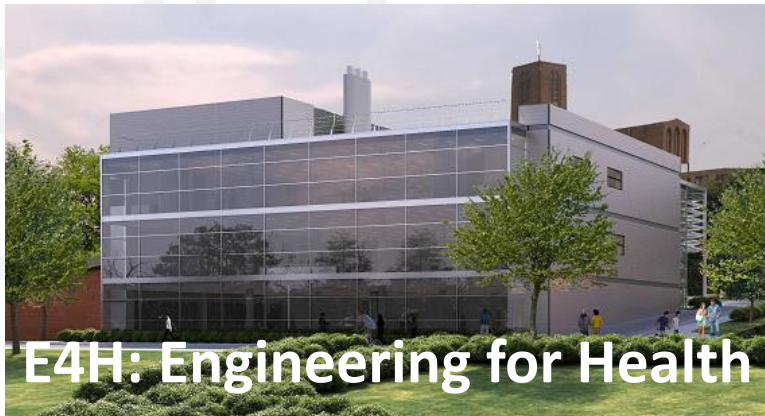
vHive: A Partnership for Innovation



Global Challenges for Animal Health

- Food security:
 - By 2050 we will have to feed 9 billion people
 - As wealth increases, demand for animal protein increases
- Disease emergence:
 - A new disease emerges every 3 months
 - 70% of these diseases are zoonoses
- Antimicrobial Resistance:
 - No new antimicrobials have been available since the 1980's
 - New strains of bacteria are resistant to all antibiotics
- Epidemics:
 - A smaller world with more people and animals enables epidemics to rage across countries, continents and the world
 - Accidental or deliberate release of epidemic pathogens

vHive:
veterinary Health InnoVation Engine



vHive: the veterinary Health innovation engine

An Open Innovation Initiative launched by the University of Surrey & Zoetis in April 2016

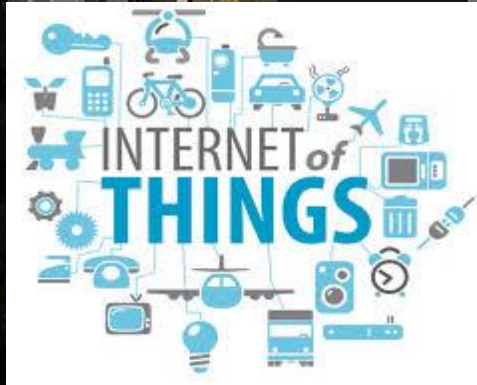
AIMS

- To promote digital innovation and use of “big data”
 - Data capture (apps, wearables, sensors etc)
 - Data integration and delivery of new information
 - Creation of new research, education and commercial opportunities



5G and the IoT

- Application and Enabler

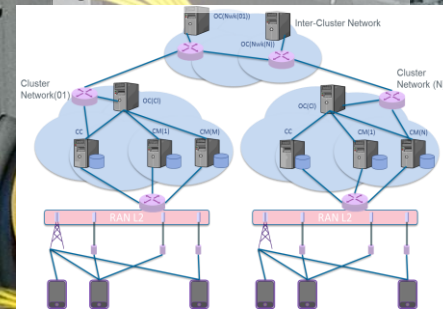


Total Investment = £85m

5G networks form the communications backbone for IoT



5G Wireless Access



IoT provides, information, data, knowledge to drive network operation

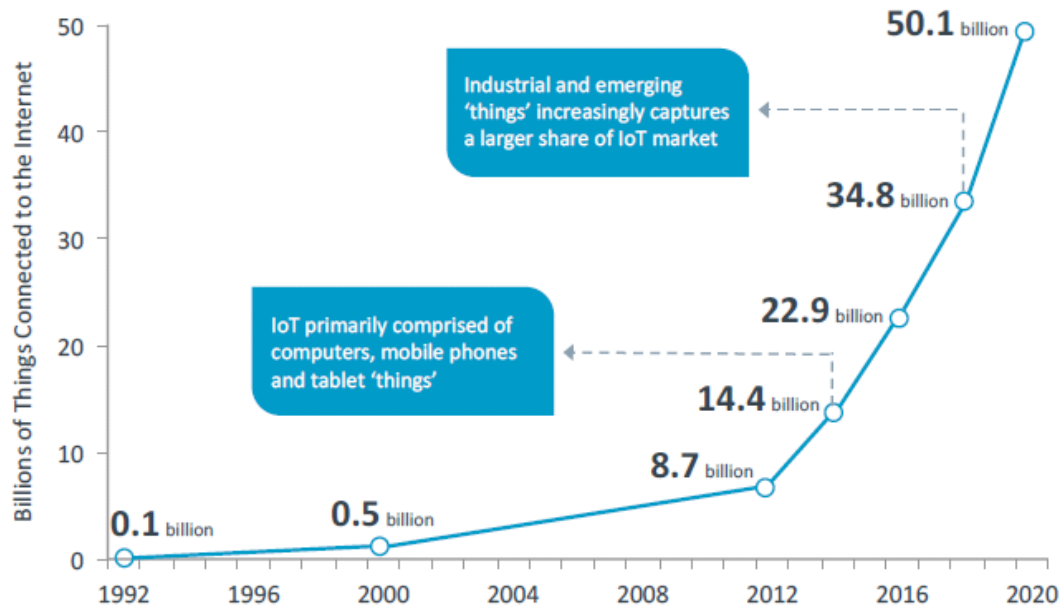


5G for IoT

- Massive connectivity

Projecting the 'Things' Behind the Internet of Things

From 2014-2020, IoT grows at an annual compound rate of 23.1% CAGR



CompTIA

Sources: Group SIR | Cisco | CompTIA

By 2020 there will be ~50 bn devices connected to the IoT

Why 5G on the farm?

- It is about connectivity rather than data rate!



Old McDonald's yard ...

Asset management

Animal well-being

To ensure animals' well-being numerous data are collected and analysed in a smart farm environment.

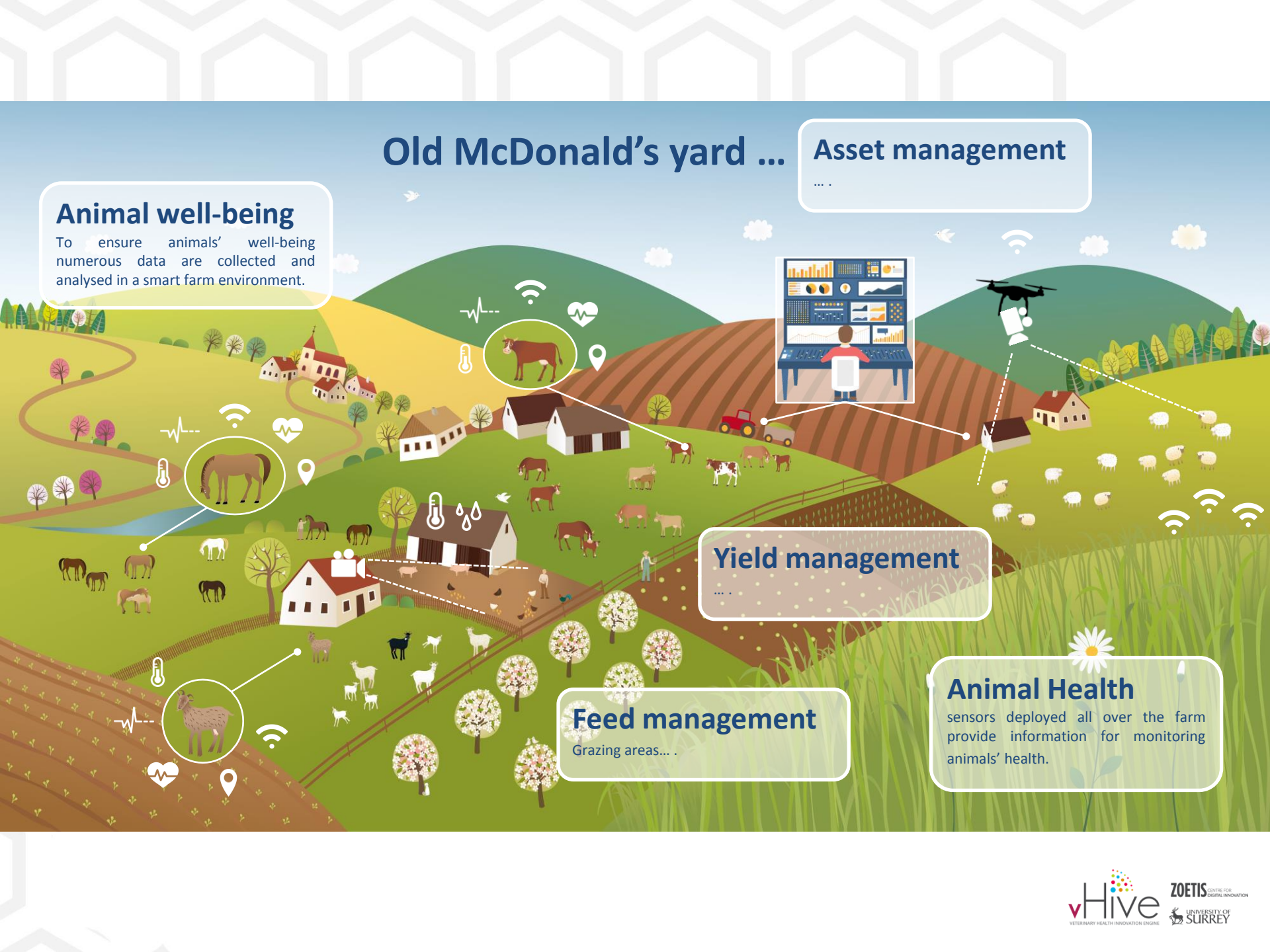
Yield management

Feed management

Grazing areas...

Animal Health

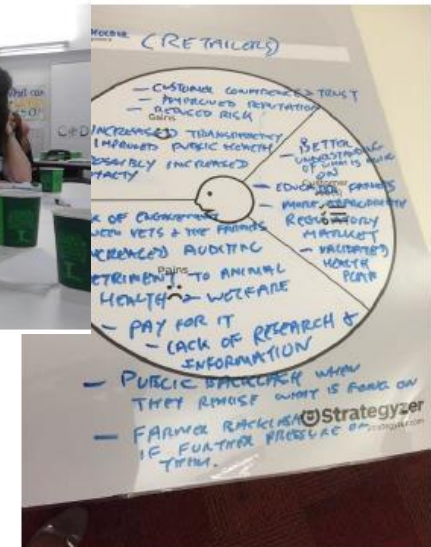
sensors deployed all over the farm provide information for monitoring animals' health.



Dairy Workshop

- What can Big Data do for you?

- Retailers
- Processors
- Producer voice (NFU)
- Agrimetrics Centre
- Vet practices
- APHA
- Socio-economists
- Researchers



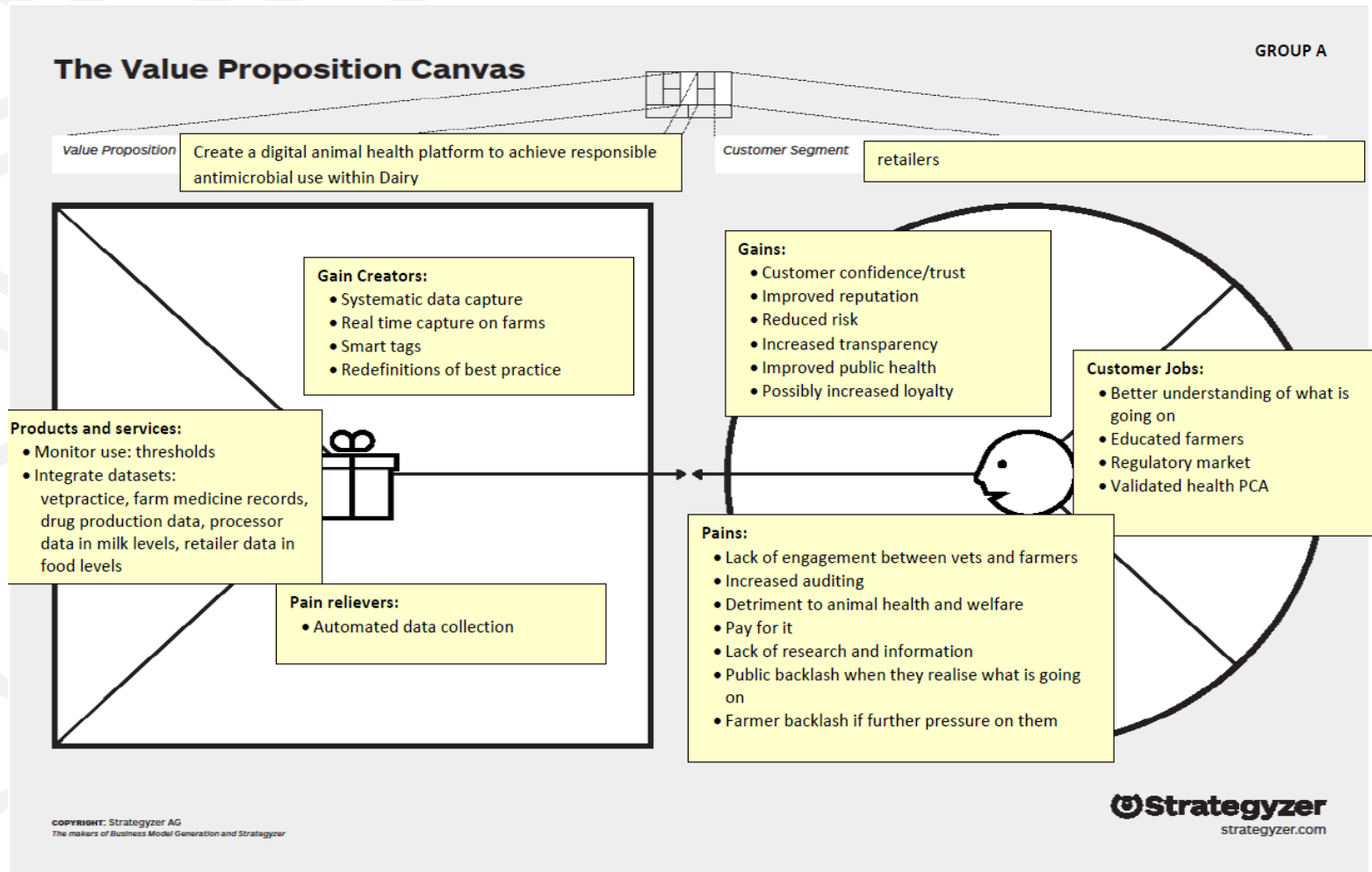
UNIVERSITY OF
SURREY



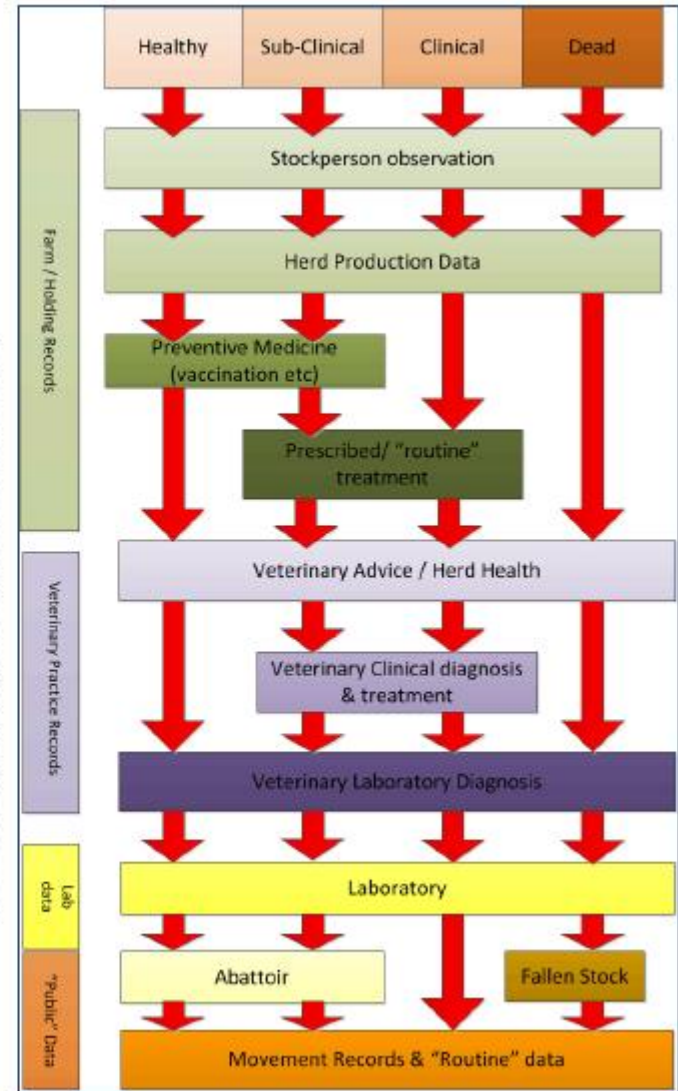
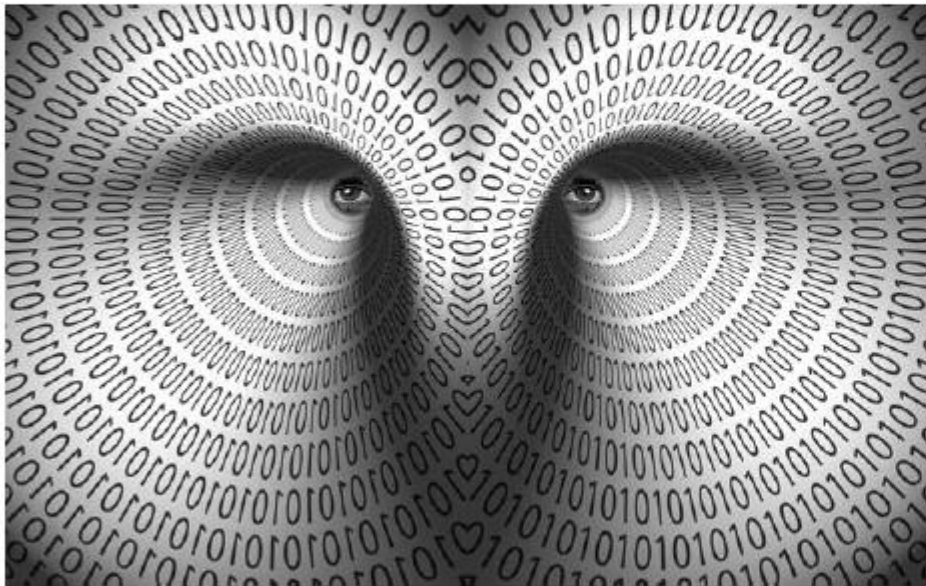
ROTHAMSTED
RESEARCH

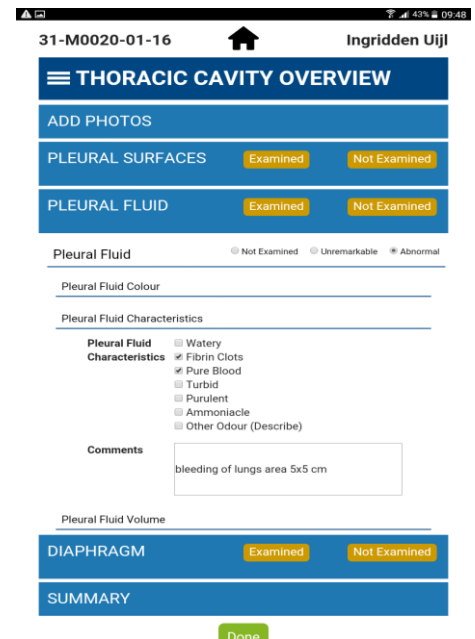
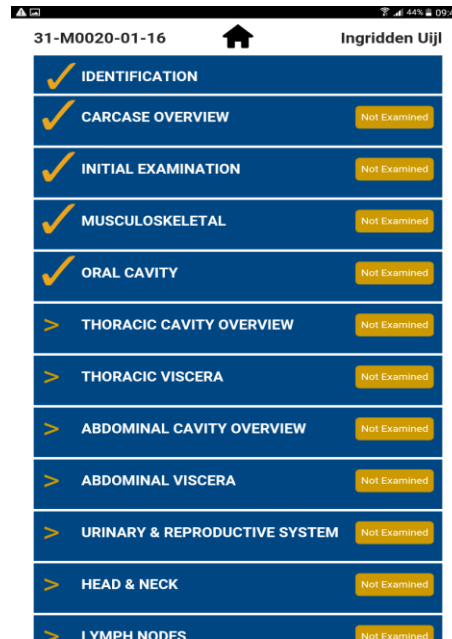
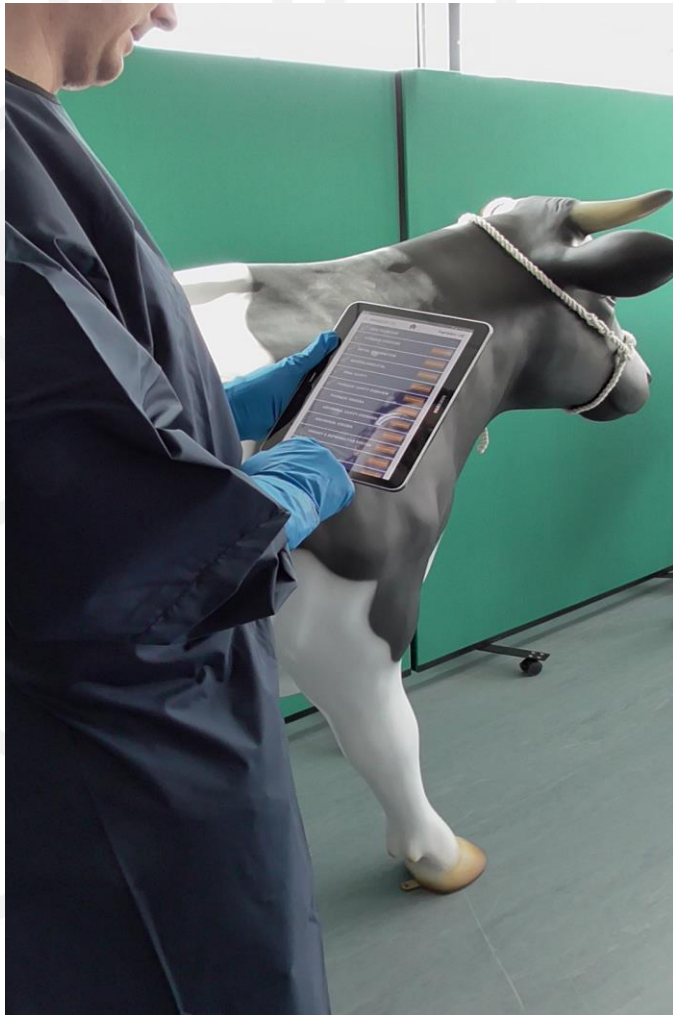


University of
Reading



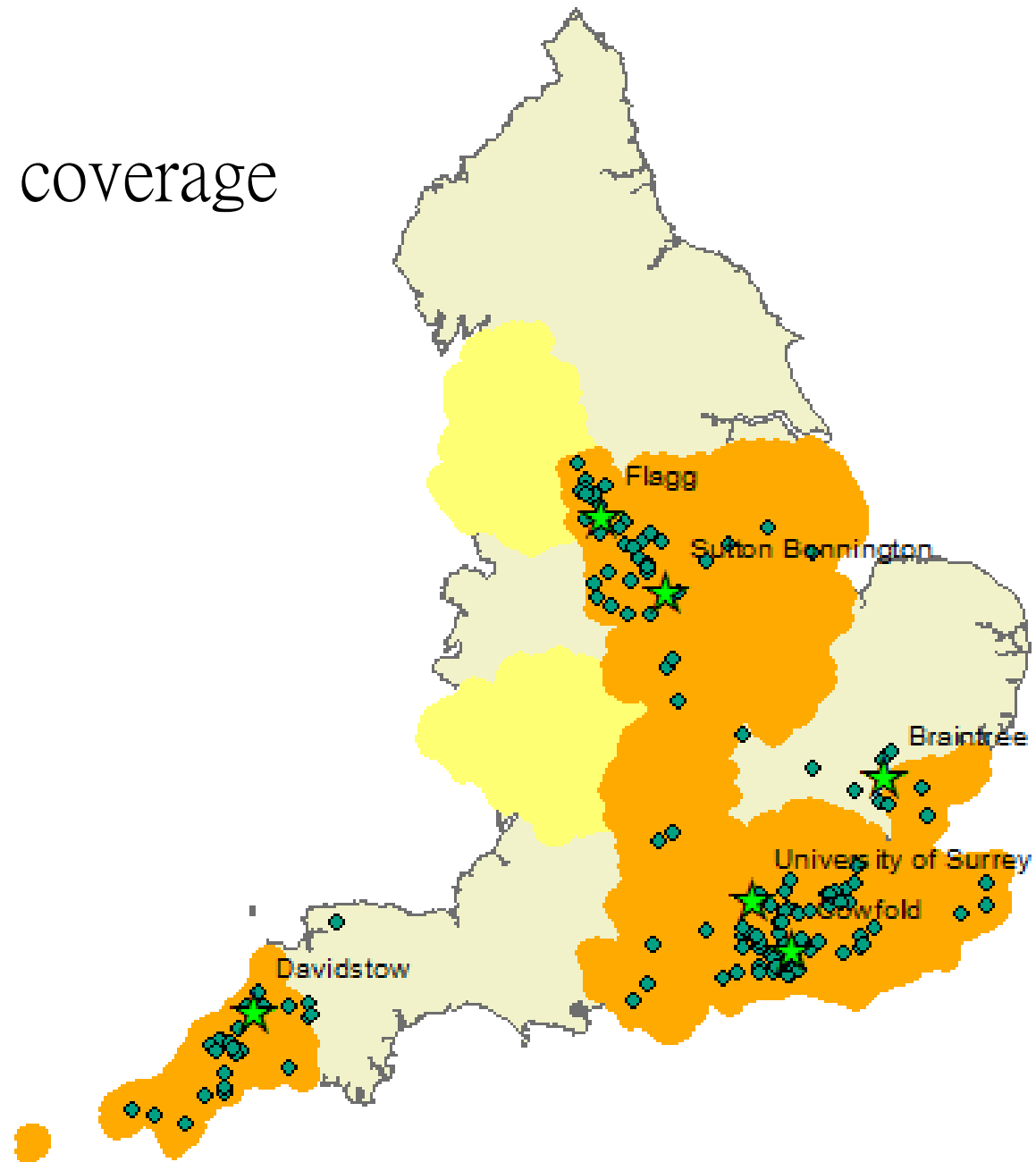
Surveillance: Intelligence for Action





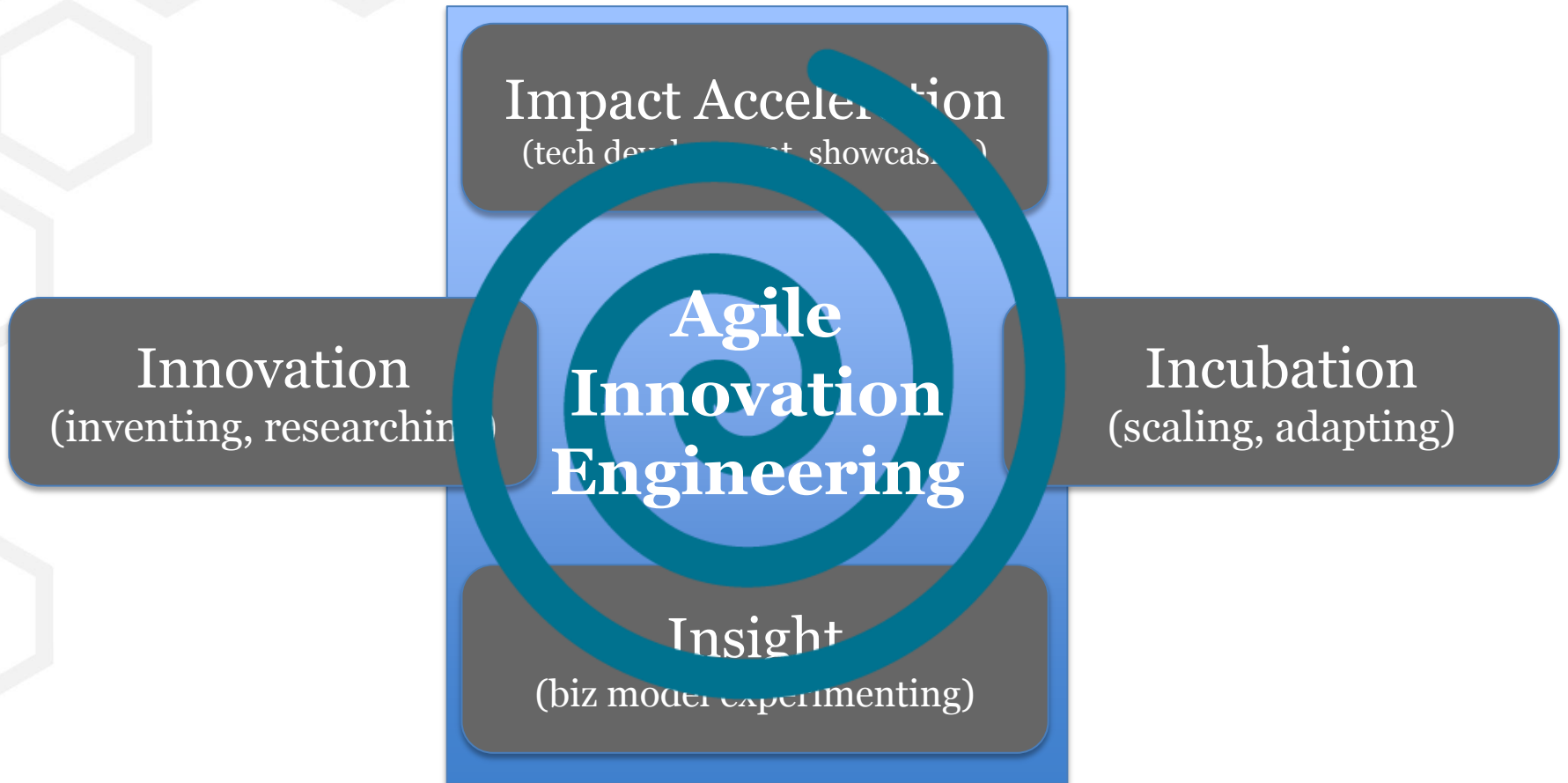
- PathPal™ is an integrated app and database for recording, analysing and reporting findings from veterinary *Post Mortem* examinations
- PathPal™ was designed by the University of Surrey and implemented in collaboration with Methods Digital

Current coverage



Bridging Invention & Innovation

Technology Readiness Levels



Focus for Digital Transformation: The 4E's Framework

Expectations

People, Communities, and Clients

Execution

Organization and Delivery

Environment

Data, Capabilities and Interfaces

Enablement

Infrastructure and Technology

All Data Great & Small



© Can Stock Photo - csp11815662



Experiences around setting up a production site to EU GMP & USDA 9CFR status in Taiwan

Romney Jackson



Structures in the Pingtung Agricultural Biotechnology Park (PABP)

Lohmann Project Yushan 禹山



Mission

Lohmann Taiwan Co Ltd was to be located in the Pingtung Agricultural Biotechnology Park, Pingtung, Taiwan. The aim was to be licensed as a biological manufacturing plant in Taiwan and to operate as under local cGMP as well as EU GMP regulations.

The purpose of the company was to capitalize on technology produced via agreements with two Taiwan-based research institutes: Animal Health Research Institute (AHRI) and Animal Technology Institute Taiwan (ATIT - now ATRI).

Commercialisation of the technologies included technical transfer to local manufacturing in the PABP site (once completed) and possibly to both the US and German vaccine sites (if/when capacities were exceeded in Taiwan).

The scope was global and included technologies for swine, poultry and waterfowl.

My Role

1. To project manage the following:

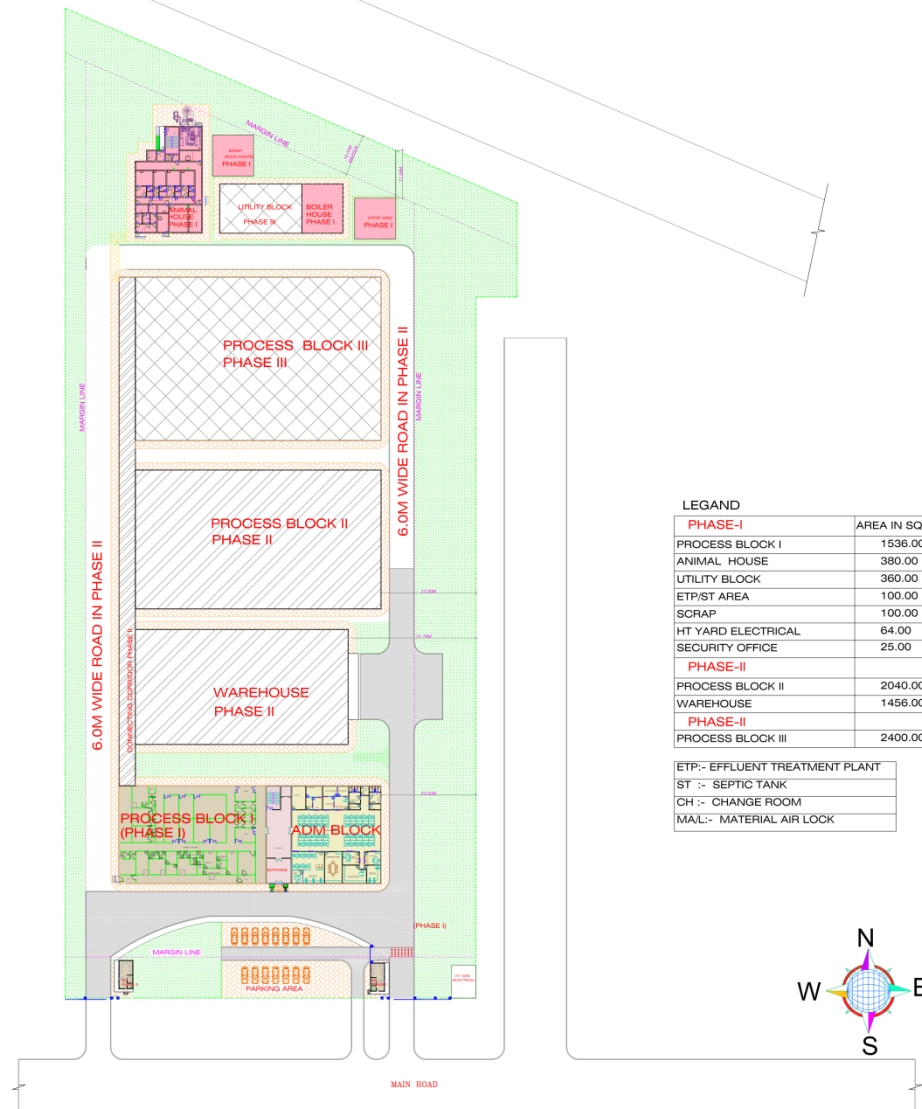
- a) The acquisition of Taiwanese research products from AHRI and ATIT (ATRI)
- b) The design and construction of a pilot facility and production unit in Pingtung
- c) To set up Lohmann Taiwan and along with a US colleague, find and employ key personnel.

2. Resources:

- a) Research acquisition was managed utilising external legal counsel and internal R&D and Regulatory input.
- b) Design and construction teams proved the hardest to select. Out of five international companies specialising in this, I selected a combination of two to manage different aspects. **One based in Germany (PIC) whose expertise was in design and manufacturing equipment and one based in India (Doshi) whose expertise was in engineering design and project management of pharma and vaccine utilities.**

**Both were very experienced in European GMP requirements.
PIC were also very experienced in 9CFR (USDA) requirements.**

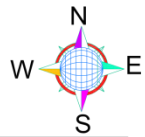
THIS DRAWING IS THE PROPERTY OF DCSPH CONSULTANTS (P) LTD. AND MUST NOT BE COPIED WITHOUT THEIR WRITTEN CONSENT NOR MADE KNOWN TO THE THIRD PARTY.



LEGAND

PHASE-I	AREA IN SQ.M.
PROCESS BLOCK I	1536.00
ANIMAL HOUSE	380.00
UTILITY BLOCK	360.00
ETP/ST AREA	100.00
SCRAP	100.00
HT YARD ELECTRICAL	64.00
SECURITY OFFICE	25.00
PHASE-II	
PROCESS BLOCK II	2040.00
WAREHOUSE	1456.00
PHASE-III	
PROCESS BLOCK III	2400.00

ETP:- EFFLUENT TREATMENT PLANT
ST :- SEPTIC TANK
CH :- CHANGE ROOM
MAL:- MATERIAL AIR LOCK



PROJECT LOCATION:- At Taiwan		CLIENT:- Lohmann Animal Health GmbH	
PROJECT:- Vaccine Block		Project Consultant DCPL International 401 Ch. Ganga, D.K. M. G. Road, #2001 Indira Park, www.dcp.com.sg/india www.dcpinternational.com	
TITLE:- SITE PLAN		Process Consultant PHC Consulting GmbH	
DESIGNER [BKD]	29.08.13	PROJECT NO.-408	SCALE:- 1:200
DRAWN [BIFAN]	29.08.13	DESIGNER [DCS]	DATE
CHECKED [BKD]	29.08.13	3/498/LOHMAN/VOL.1	V. 02
APPROVED [BKD]	29.08.13		
		NORTH	
		RELEASE FOR:-	
		COMP. REP.:- 3/498/10hh/PR./AR-001	

Pilot Plant



Animal House



Site Plan



Core Issues for the site

– **Design, work flow etc (including HVAC systems etc)**

These were managed by an engineering team based in India who took all design instructions from the work flow/design team based in Germany.

– **Equipment sourcing**

- URSs and agreed amendments (including documentation and validation)
- Validation Master Plan – Protocols, schedule, training for qualification activity. SAT.

The design team were also responsible for equipment sourcing/URSs and training and validations through to at least FAT stage.

Sourcing Manufacturing Equipment

- Sources looked at:
 - Europe (Italy, Sweden and Germany)
 - India
 - China (European companies)
 - Taiwan

URSs issued & negotiated and Sites inspected

- As we all know URSs are long detailed documents that are rarely able to be satisfied in every detail – differences have to be negotiated. Some manufacturers will manufacture to your P&IDs or at least to negotiated modifications, others will not.
- On the whole we found reasonable examples of P&IDs from Taiwanese companies but only in one company's vessels and autoclaves was there sufficient manufacturing quality to pass European GMP requirements. We found no fermenters that could meet European GMP requirements – mainly due to weld quality and the presence of double welds.
- We finally narrowed the choice down to two suppliers for each item of equipment. None of these were Taiwan-based.

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Welding URs largely failed by Taiwanese Manufacturers

UR-No.	Function	Specification	To be verified at				
			DQ	FAT	COM	IQ	OQ
	<i>System design</i>	Welding of the piping has to be carried out by orbital welding in inert gas shield.	X	X			
	<i>Piping</i>	Pipes have to be orbital welded. Welding seams by hand must be approved in advance by the customer (manual welding shall be the exception). Only qualified and certified welders with at least 3 years' experience shall be employed.	X	X			
	MOC	All components in contact with the product are made of 1.4435 / 1.4404. Surface finish: Ra < 0.8 µm, at welding positions < 1.6 µm.	X	X			

Welding:

Systems, which will be welded as part of the manufacturing and/or installation process, require the following documentation, at minimum:

UR-No.	Function	Specification	To be verified at						
			FS	DS	DQ	FAT	COM	IQ	OQ
		Welding procedure (manual, automatic): Defining techniques and test results of all vendor-proposed weld procedures for compliance with the requirements of the purchase order. Use code forms as required.		X					
		Welding machine data print out				X	X		
		Weld inspection records. Hydro Test, Spot Radiography with Category A, B and C. Liquid penetration test					X		
		Welders qualification. Qualification of all welders / welding operators using approved welding procedures and by weld position in compliance with the buyer's requirements. Code forms or sellers standard forms to be used as appropriate.				X	X		
5.10.6.1.		Welding map. Drawing showing all welds identifying applicable weld procedure.				X	X		

Equipment Choice - Examples

Fermenters: 1: Geometric Vol. 30L & Working Vol. 20L 2. Geometric Vol. 150L & Working Vol. 100L

		Sartorius India	Scigenics India
No.		Unit Price [EUR]	Unit Price [EUR]
1	Equipment Costs	398,000.00 €	166,000.00 €
2	Installation Costs (not included, local)	5,000.00 €	5,000.00 €
3	Qualification Costs (which can not be finalized during the FAT, done internally)	19,000.00 €	25,000.00 €
4	Support. Documents (done internally)	0.00 €	42,000.00 €
5	Support. Engineering	0.00 €	15,000.00 €
6	Risks	10,000.00 €	15,000.00 €
Total		432,000.00 €	268,000.00 €

Pros	<ul style="list-style-type: none"> - well established - well known - all European equipment - good supported from Germany 	- Costs & Flexibility
Cons	- Costs	<ul style="list-style-type: none"> - needs continuous support and control - poor documentation

Recommendation

We highly recommend Sartorius. Reason: in the past very good experience, best software, full European quality, minimal risks. We have reduced the costs of Sartorius taking out the qualification in Taiwan, these costs are too high. With the local internal team this could be done cheaper.

Additional Information

We have also good experience with Scigenics the quality is acceptable with a lot of additional efforts (costs), which have been included to the total amount. If Scigenics would be chosen, PAD Germany would overtake the responsibility for design and quality insured by our PAD insurance for the design.

Report Summary

Fermenters

- Technical wise both are the same, Sartorius and Scigenics.
- Sartorius has everything delivered as components from Europe and are assembling it together in India. For example: Gemü valves produced in India is used by Scigenics. Gemü walves produced in Germany is used by Sartorius. Reason the quality assurance department from Sartorius does not accept the Indian Gemü valves. Reason inside polish quality, steel quality. (price difference, half price India-Germany)
- Same for the agitator, both PRG, made in India used by Scigenics, made in Germany used by Sartorius. Reason quality assurance department of Sartorius. Small quality differences mainly in steel.
- Both are using our suggested P&ID, both are using similar components and instruments.
- Technical wise except the same.
- The software is technical different and much better by Sartorius and our experience shows that we need some efforts to reach a similar quality. Therefore the additional costs of work. Both are using Siemens S7.
- Quality wise and quality assurance wise some differences.(Scigenics has no good quality assurance department)

Filling Line: depyrogenation, filling, capping and decontamination machine - 100 x 10mL vials/min

		Snowbell India	Bosch
No.		Unit Price [EUR]	Unit Price [EUR]
1	Equipment Costs	443,846.00 €	950,000.00 €
2	Installation Costs (not included, local)	10,000.00 €	10,000.00 €
3	Qualification Costs (which can not be finalized during the FAT, done internal)	32,000.00 €	25,000.00 €
4	Support. Documents (done internal)	20,000.00 €	0.00 €
5	Support. Engineering	20,000.00 €	0.00 €
6	Risks	40,000.00 €	0.00 €
7	Additional Equipment (closed RABS/Isolator, VHP generator, LF)	285,000.00 €	285,000.00 €
Total		850,846.00 €	1,270,000.00 €

Pros	<ul style="list-style-type: none"> - price - flexibility 	<ul style="list-style-type: none"> - v experienced and well known company
Cons	<ul style="list-style-type: none"> - poor documentation - not perfect standard design - simple installations - low experience with peristaltic pump systems 	<ul style="list-style-type: none"> - delivery time - costs - flexibility

Recommendation

Snowbell India.

Reason is the price difference of 400.000€, although we have much more risks with Snowbell and support work. These costs have been included. We see a higher flexibility with Snowbell, the performance is not so good, but we need this line not very frequently and only with very little hours per year. We see also with Snowbell a much easier possibility to integrate an simple isolator on the machine.

Bosch was asking over 1.000.000€ for an isolator, but also for a closed RABS a huge amount of money. We still need on the 6th of December a final clarification meeting in India with Snowbell.

Additional Information

The filling line from Bosch is also coming from India and China. The quality will be better than Snowbell, but with the additional engineering support, we believe to come to an acceptable quality of Snowbell. We would not normally recommend Snowbell for a high performance filling line but the requirements are low in performance and batches. The RABS/Isolator from Bosch would also be supplied by a local Indian

Report Summary

Filling Line

- Technical wise exact the same, Bosch and Snowbell.
- In some details huge differences. Format pieces are normally much more précised by Bosch. Transport systems are much easier to clean by Bosch. Bosch has a huge amount of Servo motors, Snowbell has mainly one central motor for the different machines.
- The time pressure system of Bosch is very pre sized and works excellently.
- The Snowbell system is very simple but for our requirements it does its job.
- The filter systems in the tunnel of Bosch is much better, but with Snowbell we will also fulfill general requirements.
- **In summary:** expect with Snowbell a much higher rejection rate to 4%, with Bosch (our experience) 1%. But on a pilot plant machine the rejection rates has no major influence to the production costs.
- With Snowbell you can assume at least 2 hours more to change from one format to the other format (100 batches = 200hours = 4000€ per year)
- Bosch has some features by the needles at the vial washing, that Snowbell does not have. But do we really need it?

Freeze Dryer (x 2: 0.6/0.7SqM and 1.8SqM)

		Martin Christ	LSI
No.		Unit Price [EUR]	Unit Price [EUR]
1	Equipment Costs	700,000.00 €	519,000.00 €
2	Installation Costs (not included, local)	10,000.00 €	10,000.00 €
3	Qualification Costs (which can not be finalized during the FAT, done internal)	25,000.00 €	25,000.00 €
4	Support. Documents (done internal)	0.00 €	15,000.00 €
5	Support. Engineering	0.00 €	15,000.00 €
6	Risks	20,000.00 €	40,000.00 €
Total		755,000.00 €	624,000.00 €

Pros	<ul style="list-style-type: none"> - very good experience - good service - good software - very compact system - excellent components - excellent documentation 	<ul style="list-style-type: none"> - costs - flexibility
Cons	<ul style="list-style-type: none"> - price 	<ul style="list-style-type: none"> - needs additional engineering support and control - poor documentation - maintenance?

Recommendation

Martin Christ.

Reason: well known German equipment. We see much greater risk with LSI India. The price difference is not so huge.

Additional Information

Martin Christ has a very compact system with a low integrated condenser, belongs not to the top world suppliers but acceptable in quality and performance.

Report Summary

Freeze Dryer

- With the Freeze Dryers we see the highest difference of technical points.
- Christ has a patented condenser system. The condenser is under the chamber, a huge plate opens between chamber and condenser.
- LSI or Toftlon have a simple condenser connected with a mushroom valve. The advantage of the Christ systems is less air speed from chamber to condenser, less maintenance from the closing system between condenser and chamber for Christ. Christ has a very nice designed Pizza door system. The software system has several advantages to LSI, but in general technical wise both are fulfilling our URSs therefore have similar technical solutions.
- Christ needs much less technical space.

THANK YOU



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EU centralised authorisation procedures - regulatory tools to assist innovation in the EU

Dr. Faye Ioannou, European Medicines Agency, Veterinary Medicines
Department

University of Surrey, School of Veterinary Medicine,
6 September 2016





Overview of presentation

EU authorisation of veterinary medicines

Centralised procedures

Tools to assist authorisation of novel products

Vaccines



Authorisation of Veterinary Medicinal Products in the EU

3 Routes to Authorisation

Centralised Authorisation Procedure

- European Commission through the EMA/CVMP

National Authorisation Procedure

- National Authorities

Mutual Recognition/De-centralised Procedure

- National Authorities coordinated by the Coordination Group for Mutual Recognition and Decentralised Procedures (CMDv)





Legal basis for authorisation procedures

Directive 2001/82/EC as amended by 2004/28/EC

- Procedures for MRP/DCP/National authorisations

Annex of Directive 2009/9 EC lays down the technical requirements for authorisation of veterinary medicinal products, which are the same for all routes to authorisation in the EU

Regulation 726/2004

- Procedure for Centralised Authorisation

The Directive, annex and regulation all require compliance with GMP for any product produced for the EU market.

Clinical studies must be relevant to EU epidemiological situation & EU animal husbandry practices.



European Medicines Agency

- Created in 1995, established in London, UK
- Main legislation Regulation (EC) No 726/2004
- Responsibility for human and veterinary medicinal products
 - Centralised marketing authorisations
 - Guidelines for assessments
 - Scientific coordination
- In total 7 scientific Committees
- Scientific/advisory role



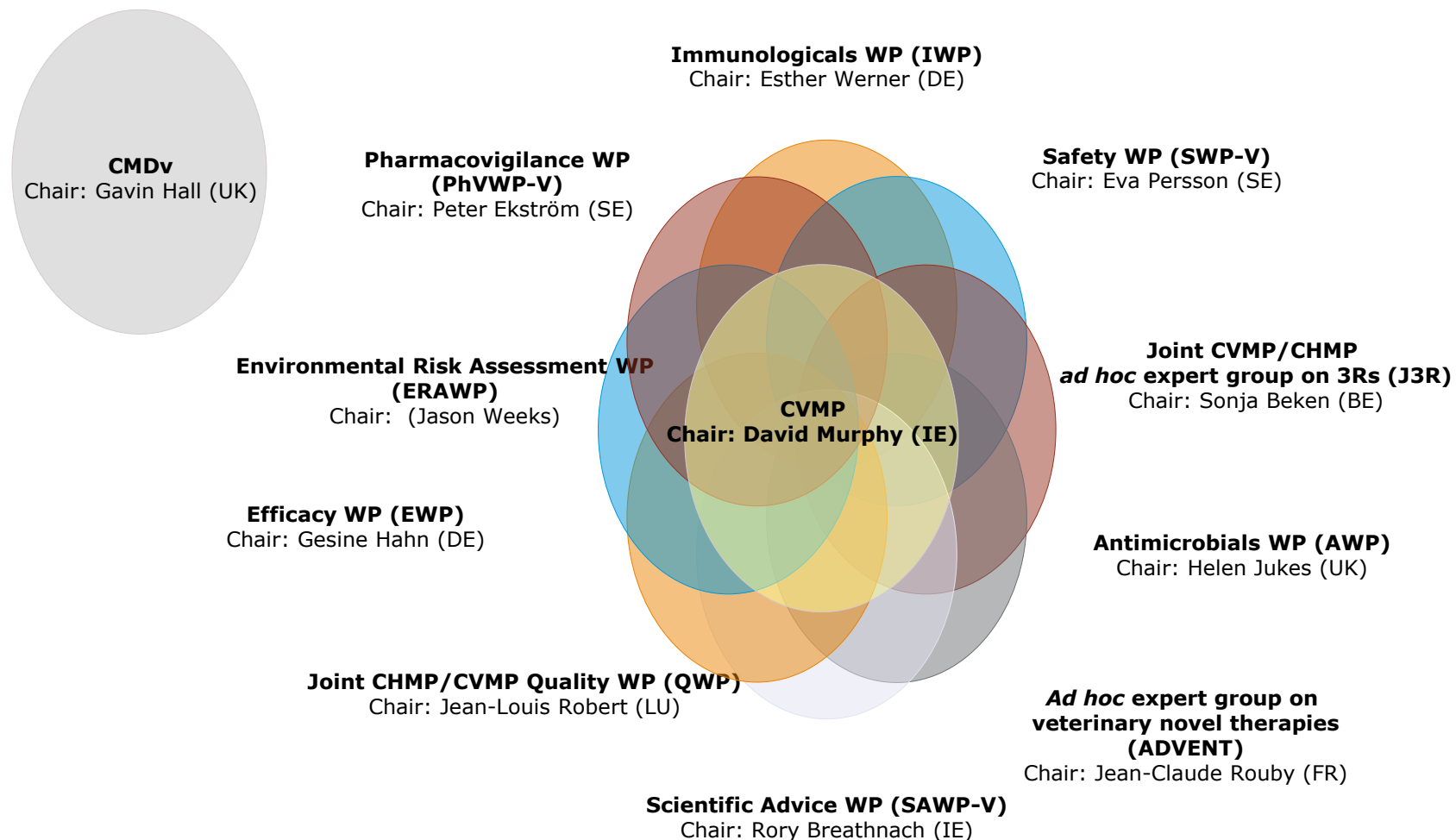


EMA Scientific Committees





Committee for Medicinal Products for Veterinary use (CVMP)





Eligibility for centralised procedure (scope)

Defined in EU legislation Regulation (EC) 726/2004

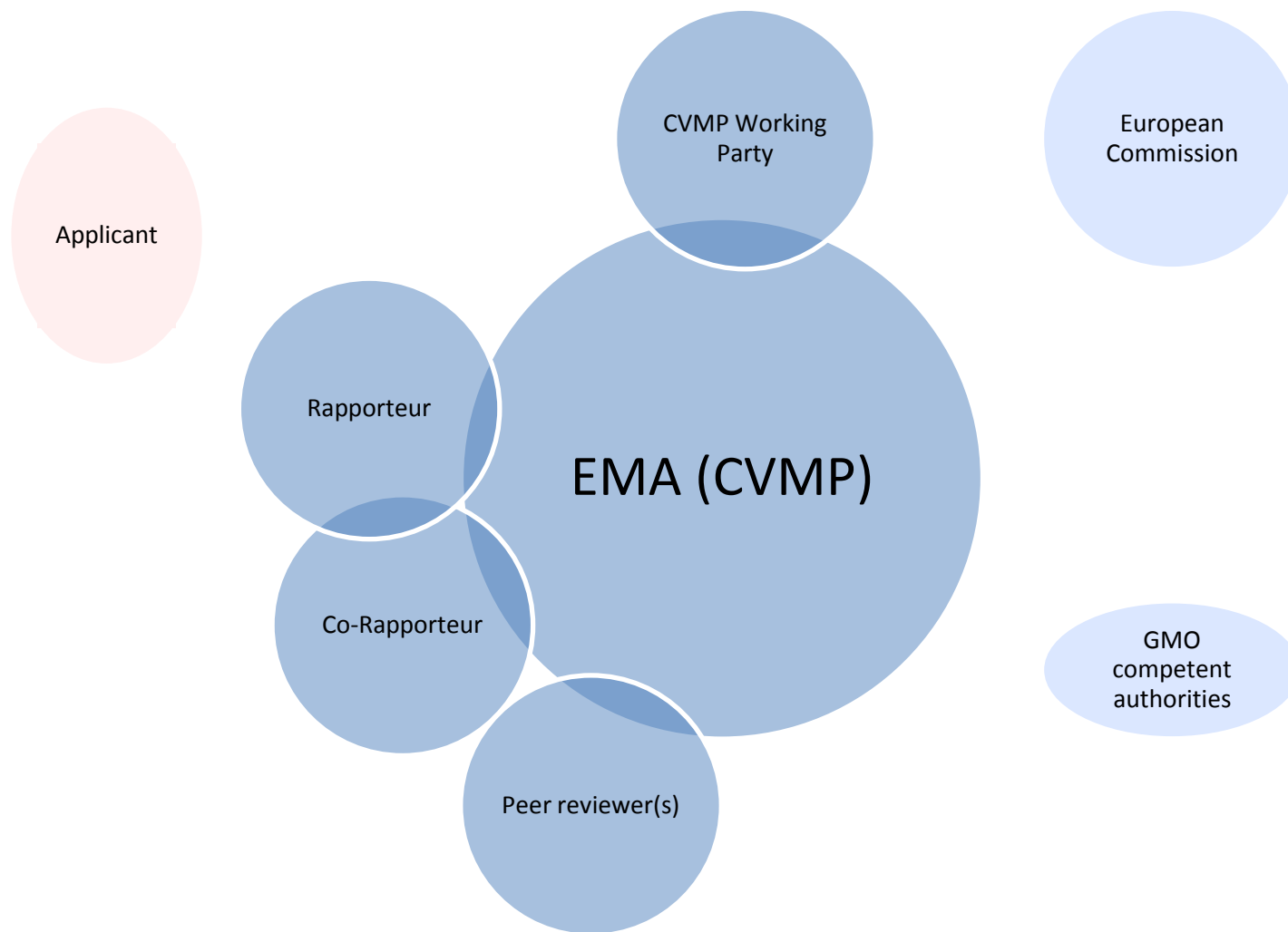
Mandatory scope: Veterinary medicinal products developed by means of a biotechnological process

- Recombinant DNA technology
- Controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells
- Hybridoma and monoclonal antibody methods
- Veterinary medicinal products intended primarily for use as performance enhancers in order to promote the growth of treated animals or to increase yields from treated animals
- Generics of centrally authorised products

Optional scope: New substances, animal health interest, immunologicals for communicable disease



Roles and responsibilities during centralised procedure



Centralised procedure in a nutshell

Pre-submission & Application:

- 1 Application to EMA

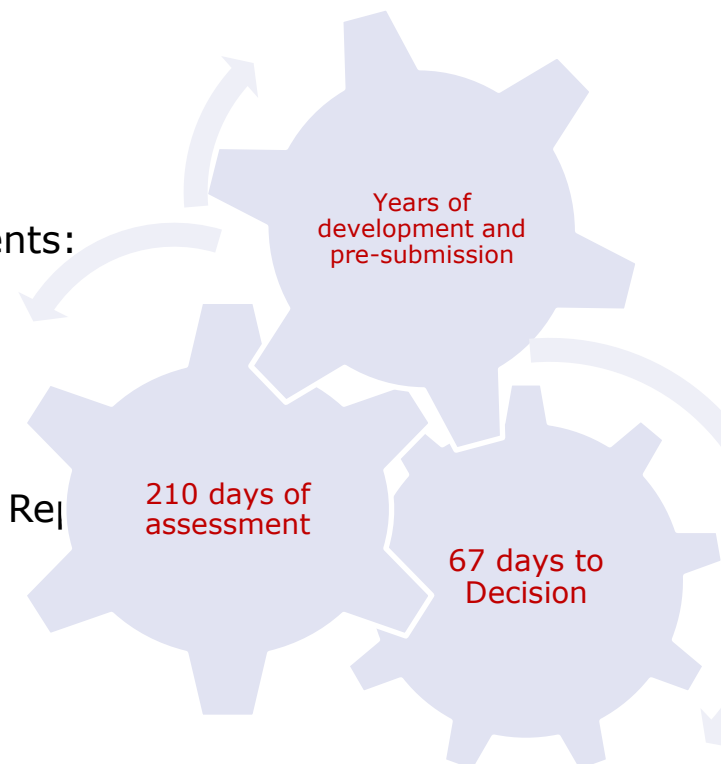
↓
Assessment by CVMP against legal and guidance requirements:

- 1 Scientific assessment
- 1 EU scientific opinion

Decision:
European Commission

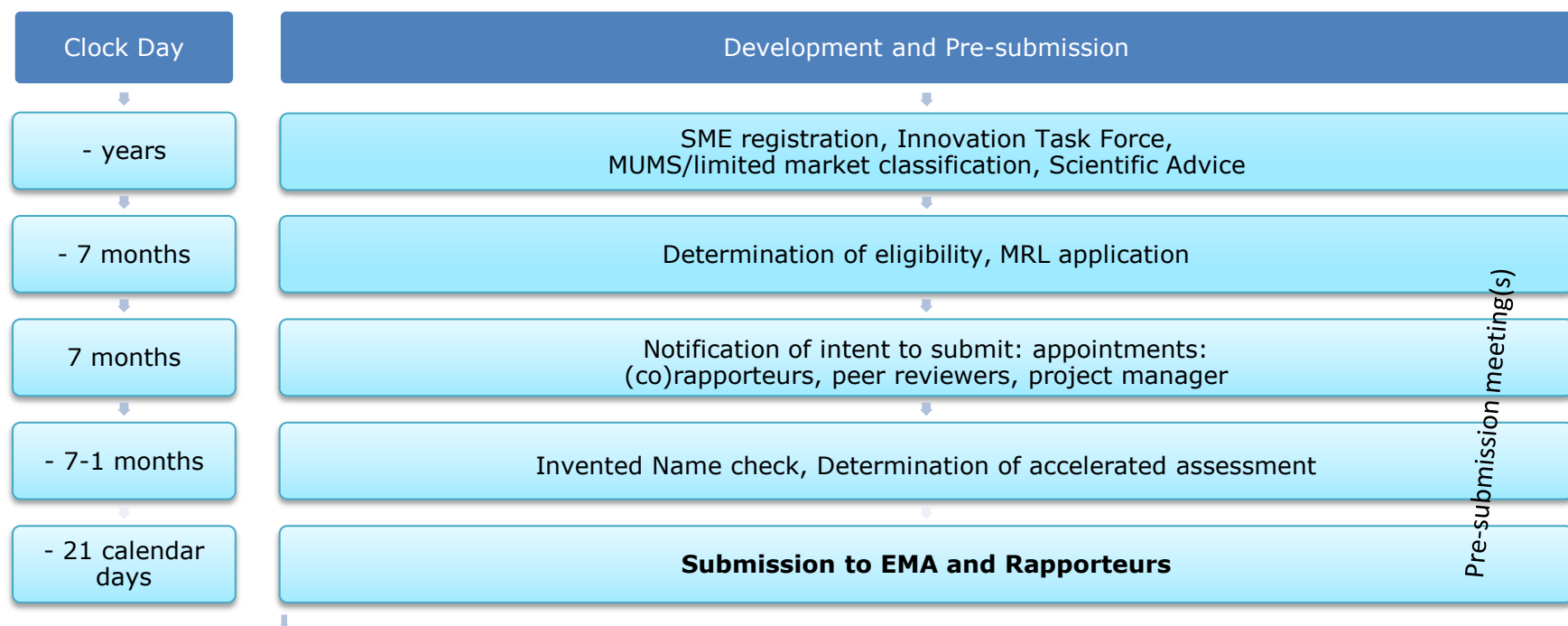
Transparency:
European Public Assessment Report

↓
Marketing authorisation:
- 1 EU-wide marketing authorisation
- applicable in all Member States + IS, NO



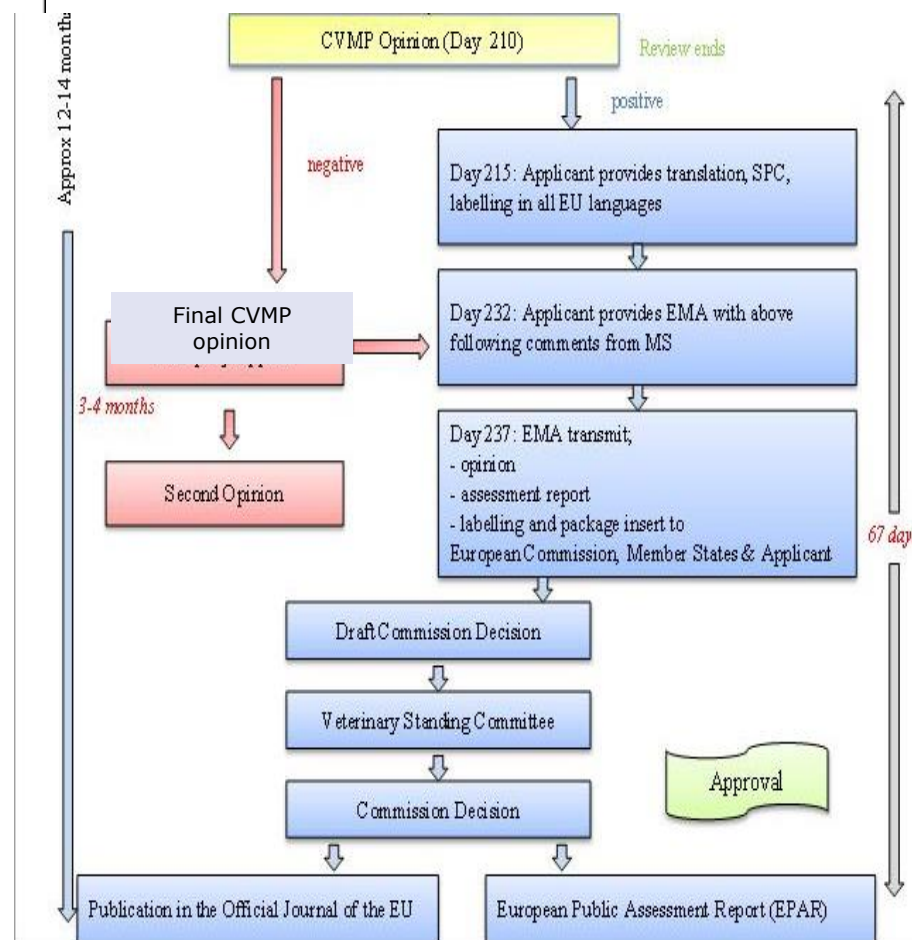
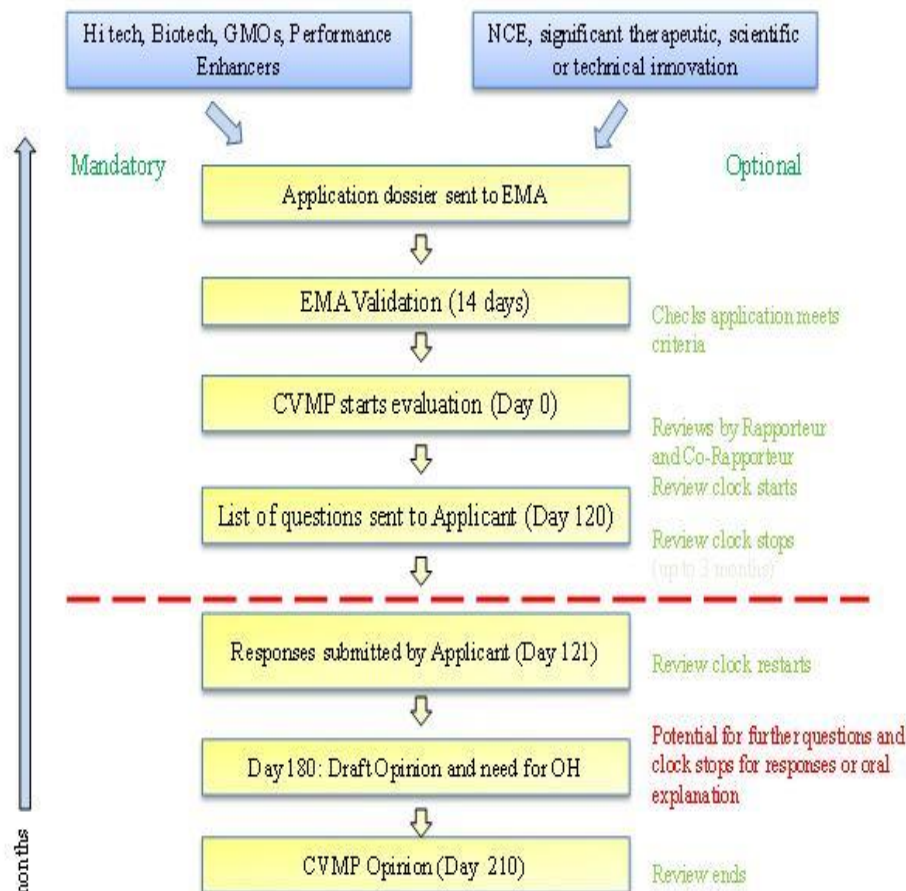


Centralised Procedure – Development and Pre-submission phase



Centralised Procedure – Timetable

Figure 1: Overview of the Centralised Procedure





Post-authorisation Procedures

- Extensions
 - Changes to the marketing authorisation on:
 - a) active substance,
 - b) strength, pharmaceutical form, administration route,
 - c) addition of target species when farm producing animals
 - Follow same procedure as initial applications
- Variations
 - Type I - minor
 - Type II - major
- Renewals
- Annual reports
- Safety surveillance, including signal detection and Periodic Safety update Report (PSUR)





Regulatory tools to assist the authorisation of innovative products

- Innovation Task Force
- Scientific advice
- MUMS/limited market classification
- SME
- Other
 - Decision on accelerated assessment
 - Exceptional circumstances
 - Fee incentives for certain epizootic diseases (i.e. BT)



Supporting SMEs

Financial and administrative assistance to small pharmaceutical companies

Innovation Task Force (ITF) Briefing

Advice on how to advance innovative medicines

Minor Use Minor Species (MUMS) market designation

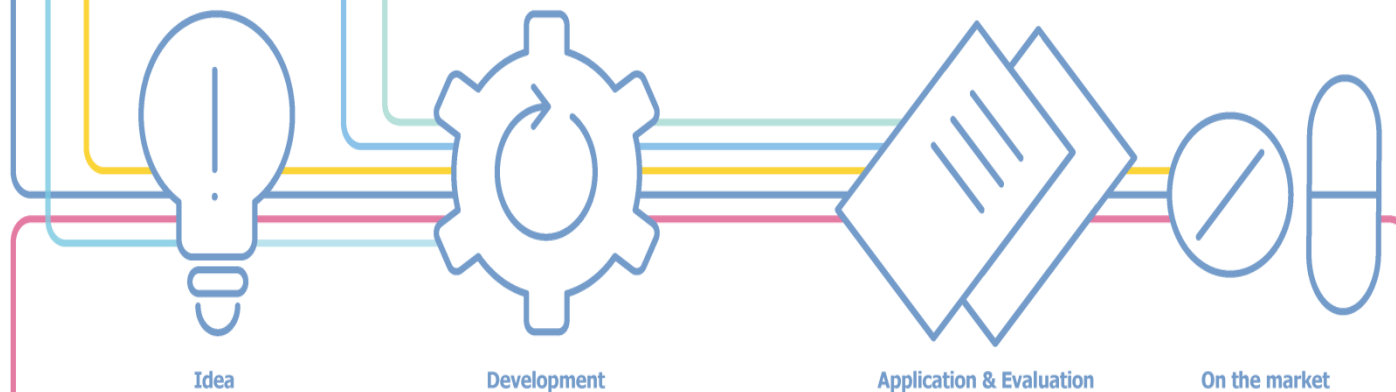
Assisting companies who develop medicines for limited markets

Scientific advice

Providing scientific advice to companies on the appropriate tests and studies in the development of a veterinary medicine

Presubmission meetings

Companies advised on regulatory questions



Ad Hoc Expert Group on Veterinary Novel Therapies (ADVENT)

European expertise to support novel veterinary medicines across the lifecycle

General guidance in support of innovation

EMA guidelines and stakeholder interaction



Innovation Task Force (ITF)

- Multidisciplinary group for preparatory dialogue and orientation with applicants on innovative medicines, technologies and methods
- Scope of the ITF activities encompasses:
 - Emerging therapies (i.e. gene therapy, cell therapy and engineered tissues),
 - Emerging technologies (i.e. new development strategies, new manufacturing approaches),
 - Borderline therapeutics (i.e. combination of pharmaceuticals and devices) for which there is no established EMA scientific, legal and regulatory experience, and
 - Biomarkers and new technology platforms

Minor use minor species (MUMS)/limited market classification

- Reduced requirements, Financial incentives food producing species only
- Definitions provided: Minor species, Minor use, Limited market



Scientific advice

- Advice to companies on questions for product-specific application dossier
- Companies ask questions as to whether their approach is acceptable
- Questions on all parts of application: MA & MRL
- CVMP Scientific Advice Working Party to give advice, adoption by CVMP
 - *Advice not binding, but in general followed*
- 60 day procedure, can be extended to 90 days

SME

- Fees incentives for scientific advice
- Fees deferral
- Assistance with translations during authorisation



Other regulatory provisions for promoting availability of needed vaccines in EU

Accelerated Assessment

- To accelerate the authorisation of veterinary medicinal products of major interest to 150d, particularly from the animal and/or public health perspective

Exceptional circumstances

- In exceptional circumstances an authorisation may be granted subject to specific measures, in particular concerning product safety,
- Limited data set for which a positive benefit-risk can be demonstrated with the data gaps highlighted on the SPC
- Continuation of the authorisation shall be linked to the annual reassessment

Fee reductions for certain epizootic diseases

- Bluetongue vaccines



Thank you for your attention

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Send a question via our website www.ema.europa.eu/contact

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AUTHORISATION OF VETERINARY MEDICINES IN THE UK

Anna-Maria Brady
B.Sc., Ph.D.
(ambbrady@btinternet.com)

- ▶ Background and history
- ▶ How the competent authorities/regulation system is arranged in the UK
- ▶ GMP/Manufacturing standards and maintenance
- ▶ What is a Marketing Authorisation?
- ▶ Control of Experimental Trials
- ▶ Import
- ▶ Batch control and batch release UK way
- ▶ Adverse reactions, environmental and quality post marketing surveillance
- ▶ Where is UK regulation now and where is it going?

INTRODUCTION

- ▶ A framework to ensure that **every batch** of veterinary medicine is **safe** for the target animal, the user, the consumer and the environment and that **it works**
- ▶ Consistent Quality, Safety and Efficacy
- ▶ Pre and post authorisation controls and monitoring

THE BASIS OF REGULATION

A decorative graphic consisting of several parallel white lines of varying lengths, slanted diagonally from the bottom right towards the top right, set against a blue background.

- ▶ 1860s British Pharmacopoeia (BP) sets quality standards
- ▶ 1950s veterinary quality standards set by BP
- ▶ **1968 Medicines Act applies to both human and veterinary medicines**
- ▶ 1995 EU harmonised Vet. Medicines Directive
- ▶ 2001 / 2009 EU Vet. Medicines Directive (currently under review).

HOW DID WE GET TO WHERE WE ARE NOW?

Established

- ❖ a **licensing authority** and an independent commission/review body
- ❖ a **licensing system** requiring scientific data to **demonstrate Q,S, & E**
- ❖ **minimum manufacturing standards**
- ❖ **regulation** of clinical trials
- ❖ **Post authorisation monitoring** of batches of products and **reporting** of adverse reactions
- ❖ **Controlled sale of medicines** by establishing categories of medicines suitable for sale over the counter or by prescription
- ❖ **Controls on import** of medicines

1968 MEDICINES ACT

GIVING

- ▶ regulatory advice to companies at early development stages
- ▶ advice to government on medicines legislation
- ▶ technical input to groups establishing medicines standards
- ▶ permission for field trials of experimental medicines

Authorising

- ▶ the marketing of medicines
- ▶ Release of batches to the market place

Post marketing surveillance of quality issues, adverse reactions and environmental incidents

Monitoring manufacturing standards and licensing manufacturing premises

Managing import of medicines

INVOLVED ACROSS THE LIFETIME OF A MEDICINE
COMPETENT AUTHORITY
ACTIVITIES

- ▶ UK vet. Medicines: The veterinary Medicines Directorate (VMD) part of the Department of environmental and rural affairs, DEFRA.
- ▶ UK human medicines: Medicines and Health products regulatory agency, MHRA part of the Department of Health.
- ▶ In some EU countries one medicines agency covers both human and vet. products e.g. Denmark, Spain,
- ▶ In Germany human and veterinary biologicals are handled by one agency and human and veterinary pharmaceuticals by a separate agency.

HOW IS THIS ORGANISED IN THE UK?



THE VMD

150 people

Vets, scientists, administrators and IT specialists

Pre authorisation and Post authorisation divisions

Two Assessment teams:
Pharmaceuticals and Biologicals

Toxicologists, environmental scientists, virologists, microbiologists, pharmacists, analytical chemists, biochemists

- ▶ Current EU legislation (2009/9) is enacted into UK legislation by the Veterinary Medicines Regulations. These also lay down the rules governing areas outwith the EU Directives.
- ▶ The EU Directive does not lay down rules for control of clinical trials, import of medicines, unlicensed special medicines.
- ▶ The EU Directive allows a member state to issue exceptional authorisations for emergency situations. These are handled in different ways by EU states.

VET MED LEGISLATION IN THE UK

- ▶ GMP is a minimum manufacturing standard implemented for all medicines authorised to be marketed
- ▶ It is a harmonised standard across vet and human medicines and it is an EU standard
- ▶ The VMD has a veterinary medicine inspection team which inspects vet pharmaceutical and bio plants across the world
- ▶ USA, Canada and Australia/NZ GMP standards are recognised for veterinary pharmaceuticals (AUS/NZ also for vet biologicals)
- ▶ Appropriate GMP is enacted for unlicensed specials and autogenous vaccines

GOOD MANUFACTURING PRACTICE (GMP)

- ▶ Approved manufacturing sites are issued with a Manufacturing certificate (MANA) which is renewed on re inspection every 5 years
- ▶ Approved Wholesale dealers are issued with a certificate (MANSA) subject to re inspection and renewal
- ▶ GMP also covers labelling and packaging sites
- ▶ Good Distribution Practice (GDP) is also covered and inspected
- ▶ VMD inspectors also look at storage of medicines within veterinary practices

GOOD MANUFACTURING PRACTICE

To sell a medicine in the UK a company must have a MA for the product

There are different procedures for different forms of MA:

- ▶ For sale in the UK only: National MA
- ▶ For sale in the UK and chosen EU states: Decentralised MA
- ▶ Converting a UK MA to UK plus chosen EU states: mutual recognition
- ▶ Certain types of medicines have to be authorised through the EMA for sale in all the EU.

WHAT IS A MARKETING AUTHORISATION (MA)?

- ▶ Q,S and E package submitted electronically in a defined format
- ▶ Within 210 days the Licensing authority and company agree a Summary of Product Characteristics (SPC), labels, a specification for the final product and final product test portfolio
- ▶ Sales category is assigned: all new actives are Prescription only medicines (POM)
- ▶ Licensing authority publishes SPC, labels and a public assessment report
- ▶ Authorised vet. Medicines have an allocated Vm/EU number published on the product literature

WHAT IS A MA?

Validation

Validated within 10 days of receipt.

Initial Assessment

Approved, refused, or questions asked within 90* days of validation passed

Company Response

If questions asked, a full company response within set deadline

Sign-off

Approved or refused by 180** days from receipt. The timescales may be suspended during this time if further information is required

Mock-ups

Mock-ups approved within 20 days from receipt of correct versions

Issue

Following approval, authorisation documentation will be issued within 10 days

UK TIMETABLE FOR NATIONAL DECENTRALISED AND MRMAS

- ▶ Some application types may qualify for reduced data packages: Abridged, Generics, Biosimilars, Minor Use Minor Species (MUMS) Informed consent, parallel import authorisations
- ▶ Informed consent, Parallel Import applications have shorter timetables
- ▶ Exceptional MAs: to fill a therapeutic gap or emergency situation: can be accelerated timetable

OTHER MA TYPES

Provisional MA

- ▶ Where there is no available medicine
- ▶ Where there is an urgent need: new disease or changing disease profile
- ▶ Allows products in last phase of development to be marketed (reduced efficacy package)
- ▶ Must be upgraded within 2 years to a full MA
- ▶ Cannot be mutually recognised
- ▶ Examples: Bluetongue vaccines, Avian Flu vaccines, Schmollenberg vaccines

HOW THE UK OPERATES
EXCEPTIONAL MAS AND MINOR
USE MINOR SPECIES
DEROGATIONS

Limited MA

- ▶ To fill a therapeutic gap where there is a niche market and small sales
- ▶ Often limited efficacy data
- ▶ Not compulsory to upgrade to MA
- ▶ Cannot be mutually recognised
- ▶ Examples: Badger BCG vaccine (*M bovis*), Gudair vaccine for sheep and Goats (*M. paratuberculosis*), Sulfratrim Oral Drops for pigeons, rabbits and bearded dragons for coccidial infection treatment (coccidian sensitive to Sulfamethoxazole, Trimethoprim)

HOW THE UK OPERATES
EXCEPTIONAL MAS AND MINOR
USE MINOR SPECIES
DEROGATIONS

EU procedures are reviewed by Member States and specific committees

UK national procedures are

- ▶ Peer reviewed at initial assessment
- ▶ Decision after company responses is reviewed by a VMD committee which includes input from ad hoc external experts & experts from other agencies (Food standards, environment, health, devolved authorities of Scotland, Wales and NI)
- ▶ Veterinary Products Committee composed of independent scientists, vets, medics and lay persons gives advice on national and EU scientific issues

ASSURING BALANCE
/IMPARTIALITY WITHIN
NATIONAL PROCEDURES

- ▶ Any clinical trial involving a veterinary medicinal product (VMP) must be conducted under a valid Animal Test Certificate (ATC)
- ▶ Trials are usually in the field in client owned animals
- ▶ An ATC lays down the conditions of conduct and ensures animal welfare standards, appropriate intervention in the case of lack of safety and efficacy and user /environment/food safety
- ▶ To obtain an ATC, the trial protocol and data demonstrating safety in the target species and environment, user & consumer if appropriate plus sufficient efficacy data to show it has a benefit plus sufficient manufacturing data to demonstrate a batch can be made

ANIMAL TEST CERTIFICATES (ATCS)

- ▶ Only national authorised products
- ▶ Apply for release of products which deviate from specification

Specific batch release of immunologicals

- ▶ Is a mutual recognition system through the network of Official Medicine Control Labs (OMCLs)
- ▶ Applies to every batch
- ▶ Review of batch protocol against agreed final product test portfolio
- ▶ UK does not re test routinely (some EU states do routinely)
- ▶ UK considers exceptions where MA conditions are still met if minor out of specifications when scientifically justified

BATCH CONTROL/RELEASE

may not always be available, or authorised in the UK to treat a range of animals and / or diseases.

In these cases, the veterinary surgeon may:

- use other products when no authorised VMP is available (the cascade)
- import authorised VMPs from other member states (SIC Scheme)
- import authorised VMPs from third countries, or human medicines authorised in other member states or third countries (STC Scheme)

- ▶ When a UK product exists, factors such as the cost of the products and the withdrawal period are not acceptable reasons to import alternatives.
- ▶ A product in a member state or third country that is not fully authorised as a veterinary medicine is subject to certain requirements to ensure it meets minimum safety

The VMD operates an on line application and issue system

IMPORT

- ▶ MA holder must report all adverse reactions to a VMP and environmental issues to the licensing authority
- ▶ Vets and owners can also report
- ▶ MA holders must report all batch product defects to the licensing authority
- ▶ The licensing authority can withdraw or suspend a MA based on adverse reactions and batch defects
- ▶ The licensing authority can demand withdrawal of specific batches from the market

POST AUTHORISATION CONTROLS

1968

- ▶ Inspection of all manufacturing sites every 2 years
- ▶ All applications for novel combinations, new actives, new species exceptional MAs referred to the VPC automatically
- ▶ Routine testing of batches before release to the market
- ▶ MA subject to 5 year renewal

NOW

- ▶ Risk based inspection: sites with minor issues inspected less frequently
- ▶ MA applications only referred to VPC when specific scientific advice sought
- ▶ Risk based assessment: Limited review of “also ran” products through Decentralised/MR procedures
- ▶ Administrative batch release of vaccines routinely & specific batch control of pharmaceuticals
- ▶ No assessment of EU imported medicines
- ▶ Limited renewal assessments

WHERE ARE WE NOW?

EU legislation review:

More harmonisation through one regulation, increased EMA control

Reduced regulatory burden through pragmatic quality standards, more flexible technical requirements, fewer post authorisation obligations and monitoring?

Risk based assessment and inspection

WHERE WE ARE GOING?

A decorative graphic consisting of several parallel white lines of varying lengths, slanted diagonally from the bottom right towards the top right, set against a blue background.

Challenges to the traditional pharm/immuno product split

- ▶ Cell based products/therapies
- ▶ Biologicals: biological source materials and manufacture/pharmacodynamic mode of actions
- ▶ Phage therapy (against multi drug resistant bacteria)
- ▶ Gene therapies –personalised medicines

Control of Anti Microbial Resistance

Harmonised EU control?

Global markets/harmonised global requirements

**WHERE ARE WE GOING?
CHALLENGES TECHNICAL AND
OTHERS**

THANK YOU FOR
LISTENING !
ANY QUESTIONS?



- ▶ Head of Immunologicals and Inspections VMD 2008-9
- ▶ Head of Biologicals and Administration VMD 2009-2016 (May)
- ▶ UK Alternate to CVMP 2008-2016 (May)
- ▶ Member of CVMP Scientific Advice Working Party (2008-2016 (may)
- ▶ UK member of European Pharmacopoeia Group 15V (vet vaccines) 2007-current
- ▶ Chair British Pharmacopoeia Veterinary Vaccine Panel 2010-current
- ▶ Member of British Pharmacopoeia Biologicals group 2016 Current
- ▶ Member of the British Pharmacopoeia Commission Current

SUMMARY BACKGROUND INFORMATION ON THE SPEAKER



**INNOVATION
IS**

GREAT

BRITAIN & NORTHERN IRELAND

Propelling Agri-Tech Innovation

**Dr Simon Doherty BVMS CertAqV MRCVS CBiol FRSB
UKTI Agri-Tech Organisation**



2 billion more people

The world's population is expected to rise from 7 to 9 billion by 2050... and could reach 11 billion by 2100



The World Health Organization estimates that one third of the world is well-fed, one third is under-fed and one third is starving. By 2050 that number could be significantly larger when the world's population is expected to reach a whopping 9 billion. The world's driest regions in Northern Africa and the Middle East are also the fastest growing, putting them at an especially high risk of furthering the food crisis.

WORLD POPULATION GROWTH
FROM 2008 TO 2050

Diets are changing...

More **meat** and **dairy** products are being consumed





... effects on land, energy, water, feed, fertilisers and other resources

Agriculture is competing for resources

Urbanisation and **industrialisation** put more pressure on land





Agricultural Technologies

The key to feeding and fuelling the planet



Agricultural Technologies

The key to feeding and fuelling the planet



Companion animals

Growing global population allied to growing human population



Companion animals

Significant health & welfare challenges



UK Context



Agriculture employs **450,000** people.



Agriculture contributes **£9 billion** to the UK economy and underpins the UK's **£26 billion** food and drink manufacturing sector.



UK Industry Overview

The UK is one of the top 12 food and drink exporters



£18 billion

£18 billion of food, feed and drink exports in 2012



£900 million

The European Commission is a significant funder of research. Horizon 2020 has committed **£900 million** and agri-tech funding

3.8 million people employed in the Agri-food chain



£9 billion



UK agriculture employs **450,000** and contributes **£9 billion** to economy

£96 billion

worth **£96 billion** (7% of GVA)

£450 million

spent on agri-food R&D (2011-2012) by UK Government funded bodies (e.g. TSB and BBSRC)

\$4 billion

Combined spend on agricultural R&D by 13 western European economies is **\$4 billion**



Department for International Trade

UK Context

The UK boasts three specific strengths

The Government's UK Strategy for Agricultural Technologies will ensure these elements work together to enhance the UK's world-leading position.

- 1 World-class science
- 2 Progressive food and farming supply chain
- 3 Dynamic business environment



UK Industry Sectors

The UK Agri-Tech industry comprises four key sectors:

- Plant Science
- Precision Agriculture
- Animal Science
- Aquaculture



UK Strategy for Agricultural Technologies

UK Government is working with science base, and food and farming industry so the UK can:

- become a world leader in agricultural technology, innovation and sustainability;
- exploit opportunities to develop and adopt new and existing technologies, products and services to increase productivity; and thereby
- contribute to global food security and international development by ensuring safe, healthy, nutritious food is affordable and accessible to all.



UK Strategy for Agricultural Technologies

- **Built on existing £450 million Government research funds**
- **Established an Agri-Tech Organisation**
 - To promote foreign trade & investment in R&D and Agri-Tech Companies
- **Pledged £90 million for world-class Centres for Agricultural Innovation**
 - To support the wide-scale adoption of innovation, technologies & skills
- **Created a £70 million Agri-Tech Catalyst**
 - To translate research into business
 - Includes £10m for developing countries

Agri-Tech Catalyst
Helping to commercialise
UK agricultural innovation



Animal Health Developments

Productivity
Environmental Impact
One Health
Diagnostics
Nutrition
Welfare
Genetics
Surveillance
Use of Medicines
Sustainability

Focus on Animal Sciences

Development of products and services relating to animal health & welfare; including those related to the prevention, detection, characterisation, management and treatment of animal diseases and animal health.



The UK is the easiest major economy in Europe to do business in

- UK Veterinary Science ranks worldwide at No2, with 67% increase in funding
- More international animal disease reference centres than any other country
- Edinburgh has largest concentration of animal health researchers in Europe



Yearly growth in UK veterinary research publication output at 6% is twice that of the US.

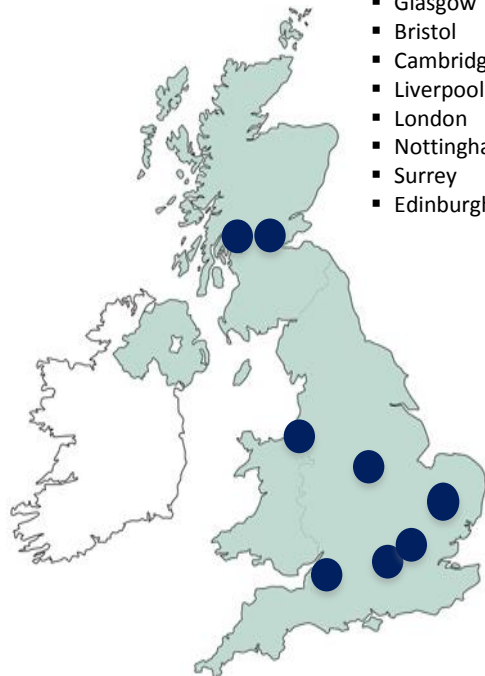


£601 million

The market for animal medicines in UK was approx. £601m in 2014, an increase of 61% from 2005.



Around 55% of animal medicines are used for companion animals



- Glasgow
- Bristol
- Cambridge
- Liverpool
- London
- Nottingham
- Surrey
- Edinburgh

The UK boasts investment from major global animal health companies.

- Abbott Animal Health
- Bayer
- Benchmark Vaccines Ltd
- Bimeda
- Boehringer Ingelheim
- Ceva
- Chanelle
- Dechra
- Elanco
- Idexx Laboratories
- Merial
- MSD Animal Health
- Neogen
- Neptune
- Norbrook
- Vetoquinol
- Virbac
- Zoetis

Animal Science Specialist:
Simon Doherty
BVMS MRCVS FRSB



Focus on Aquaculture

World class research

The UK is world renowned not just for world class agri-tech R&D, but its proven ability to develop and bring, with commercial partners, new products and solutions to market for improving the efficiency of aquaculture production.

- **The Centre for Environment Fisheries and Aquaculture Science (CEFAS)** is the UK's largest and most diverse applied marine science centre, with capability covering shelf sea dynamics, climate effects on the marine environment, ecosystems and food security. Through CEFAS Technology Ltd, a number of innovations including the CEFAS Mooring Locator and Data Storage tags have been developed for the industry.
- **The Scottish Aquaculture innovation Centre (SAIC)**, based at the University of Stirling combines cross-disciplinary research on environments, reproduction, genetics, aquatic health, nutrition and feed supplies on production systems and markets, as well as social and economic impacts on the wide range of challenges faced as aquaculture grows to meet global demands. It also develops platforms for testing fish health and veterinary products, including challenge models.
- **The Centre for Sustainable Aquatic Research** based at Swansea University, Wales, is equipped with modern, fully programmable recirculating aquaculture systems, designed for applied research on a diverse range of aquatic organisms, from temperate to tropical and marine to freshwater environments.
- **Hull International Fisheries Institute** is a specialist unit at the University of Hull that undertakes a range of research, education, training and consultancy in fisheries, conservation and aquatic-resource management.

The UK is the leading aquaculture producer by value, within the European Union



Fresh salmon is exported to over 50 countries

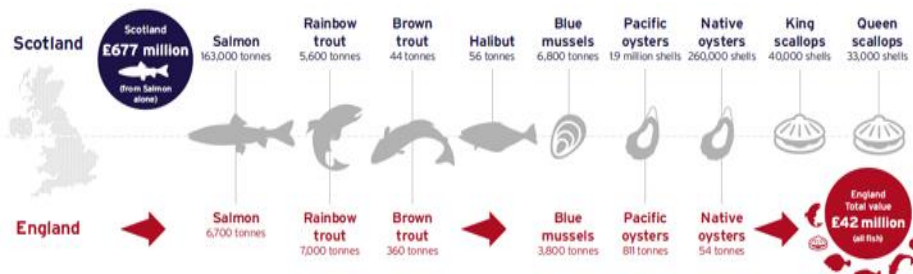


The UK has the world's largest algal bio-fuel project (£26 million) to develop transport fuels from algae by 2020

£26m



Every new fish farm contributes an average of £10.5 million per annum to the UK economy



8 GREAT Technologies

The 'Innovation is GREAT' campaign seeks to:

- highlight UK technology & innovation
- promote UK as a partner of choice
- build and commercialise new technologies and products
- unlock trade and investment opportunities

SPACE
**SYNTHETIC
BIOLOGY**
ROBOTICS
AND
AUTONOMOUS
SYSTEMS
**BIG
DATA**
AGRI-TECH
ADVANCED
MATERIALS
REGENERATIVE
MEDICINE
ENERGY

Thank you

Simon Doherty BVMS CertAqV MRCVS CBiol FRSB

Specialist, Animal Sciences & Aquaculture

Agri-Tech Organisation

Department for International Trade

1 Victoria Street, London, SW1H 0ET, UK

M: +44 (0) 7881 002646

E: simon.doherty@trade.gsi.gov.uk





origin

The source of animal insight

Poultry disease control

Keith Warner BVM&S Bsc(Vet sc) Hons MRCVS
Monogastric Livestock Director

Origin is an evidence-based animal health business, able to serve the demands of our customers, whilst developing our people to fulfil their potential.

We deliver a range of veterinary, laboratory, research, consultancy and training services to production animal producers, livestock farmers, government and corporate clients.

Our vision is to ensure the optimal health, welfare and production of all the animals under our care, by offering our clients access to world class knowledge, information, services and products.



The source of animal insight

The source of animal insight **originanimal.com**





RETFORD POULTRY
PARTNERSHIP LTD



UK Poultry Industry

- Over 930 million meat birds in 2015.
- Based on sales of £6.9 billion in 2014, the poultry meat industry made a £3.6 billion gross value added contribution to UK GDP.
- The industry supports 79,300 jobs in the UK – 34,800 direct, 29,400 in the supply chain.
- By weight, poultry makes up around half of all meat purchased in the UK.

UK Poultry Industry

- 900M Broilers
 - 35M Layers
 - 40M Game
 - 17M turkeys
-
- Origin - We look after around 220 million Broilers and 1M Broiler parents, 4 million turkeys (hatchery and rearing) + the 90K breeders that produce them, 3 - 4 million layers in lay, 18M commercial layers in hatchery, 1.7M layers in rear. Game is very difficult to know, but 10 million may not be a silly guess.

Broilers

- Cargill Meats Europe – 100m broiler chickens p.a.
- Faccenda – 100m chickens, turkeys and ducks
- Hook 2 Sisters / 2 Agriculture – 300M broiler chicken pa
- Moy Park – 120m in GB (+120m in NI)
- Rest is Crown / Banham / Independents

Layers

- Parents through EW group
 - Aviagen
 - Lohmann GB
 - Hyline
- And Tom Barron
- Major egg packers will be Noble, Stonegate and John Bowler

Turkeys

- Bernard Matthews
- Faccenda Turkeys

Traditional Veterinary Role

- “Fire Brigade” response to problem
- Autopsy and further sampling to reach diagnosis
- Treat affected birds
- Create health plan for future prevention
 - Vaccination
 - Prophylactic medication

Diseases

- No notifiable disease
- Endemic diseases – IBD / IBV / AmPV – all very well controlled with vaccination strategies
- Enteric disorders
- Nutritional / metabolic disturbances
- Stress related secondary E. coli

Progression of Veterinary Role

- Advise on management
 - Ventilation
 - Hygiene and biosecurity
 - Water hygiene
 - Stress avoidance

Changing environment

- AMR – no prophylaxis
- Renewable energy – RHI - broilers
- Welfare – public perception vs science vs production
- Food safety – real and perceived

Opportunities - data

- Develop systems to collect and analyse data
- Clinical and production
- Marry the two
- Targeted approach to improvement based on benchmarking

origin



The source of animal insight

CORPORATE OVERVIEW

September 2016





TODAY'S AGENDA

- Introduction to Zoetis
- Industry Overview
- Company Overview
- How We Deliver Value

zoetis

Our name has its root in *zo*, familiar in words such as zoo and zoology and derived from *zoetic*, meaning “pertaining to life.”



Building on more than 60 years of experience, Zoetis discovers, develops, manufactures and markets veterinary vaccines and medicines, complemented by diagnostic products and genetic tests and supported by a range of services.

OUR HISTORY AND HERITAGE

Pfizer researchers discovered Terramycin, marking our entry into animal health



Launched Liquamycin LA 200

Acquired SmithKline Beecham's animal health division

Launched Draxxin, Convenia, Cerenia, Palladia and Improvest



Established vaccine manufacturing capabilities in China

Pfizer sold minority stake in Zoetis. Zoetis became a standalone company.

1950 1952 1980 1990s 2000s 2012 2013

Animal Agriculture division formed; renamed Pfizer Animal Health in 1988



Launched Dectomax, Rimadyl, Clavamox and Revolution



Acquired Pharmacia Corporation and CSL Animal Health

Established dedicated R&D headquarters in Kalamazoo, Mich.



Acquired Embrex Inc., Catapult Genetics, Bovigen LLC, Wyeth and Fort Dodge Animal Health, Vetnex Animal Health Ltd., Microtek International Inc., Synbiotics Corporation, King Pharmaceuticals Inc. and Alphaarma

Pfizer announced that its Animal Health business will become a standalone company called Zoetis



OUR HISTORY AND HERITAGE (CONT'D)

Launched Apoquel® in the U.S. and Europe

Received full license for first vaccine for Georgia 2008 type infectious bronchitis virus in poultry.



Named a top 10 company on *Working Mother* magazine's "100 Best Companies for Working Mothers" list in 2014 and 2015.



Acquired the animal health assets of Abbott

Granted USDA conditional license for Canine Atopic Dermatitis Immunotherapeutic



Enhanced Manufacturing and Supply network with expansions in Lincoln, Neb. and Suzhou, China.



Acquired PHARMAQ, the global leader in vaccines and innovation for health products in aquaculture.

PHARMAQ

2014 - 2015

Held first Annual Meeting of Shareholders in Short Hills, N.J.



Granted USDA conditional license for porcine epidemic diarrhea virus (PEDv) vaccine.

Held inaugural Investor Day at the New York Stock Exchange



Embarked on 18-month operational efficiency plan to simplify operations, improve cost structure and better allocate resources to key growth opportunities.



Acquired KL Products, Inc., a leader in automation systems for the poultry industry

Received European Commission approval for Simparica™.



28 MANUFACTURING SITES

8 CORE ANIMAL SPECIES



\$4.8

BILLION

ANNUAL REVENUE

APPROXIMATE R&D COLLEAGUES

1,050

300 APPROXIMATE NUMBER OF PRODUCT LINES

WE PROVIDE

MEDICINES
VACCINES
DIAGNOSTICS
GENETIC TESTS
SERVICES

60+ YEARS OF EXPERIENCE

5 MAJOR PRODUCT CATEGORIES

MARKET PRESENCE IN
100+
COUNTRIES

APPROXIMATE COLLEAGUES WORLDWIDE

9,000

OUR FOCUS

37%¹

COMPANION ANIMAL HEALTH

62%¹

LIVESTOCK HEALTH

2,800

APPROXIMATE FIELD FORCE MEMBERS

Note: Facts and figures shown are as of Dec. 31, 2015 | ¹Excludes revenue associated with Client Supply Services, which represented 1% of total 2015 revenue.



INDUSTRY OVERVIEW

THE ANIMAL HEALTH INDUSTRY

The animal health industry works with two important segments: livestock health and companion animal health.

- **LIVESTOCK HEALTH** focuses on the production of high-quality food for an expanding population in a world of finite resources.
- **COMPANION ANIMAL HEALTH** focuses on the treatment and care of pets so they can live longer, healthier lives.

Products, services and complementary businesses within our industry help customers keep the animals in their care healthy and their operations successful.



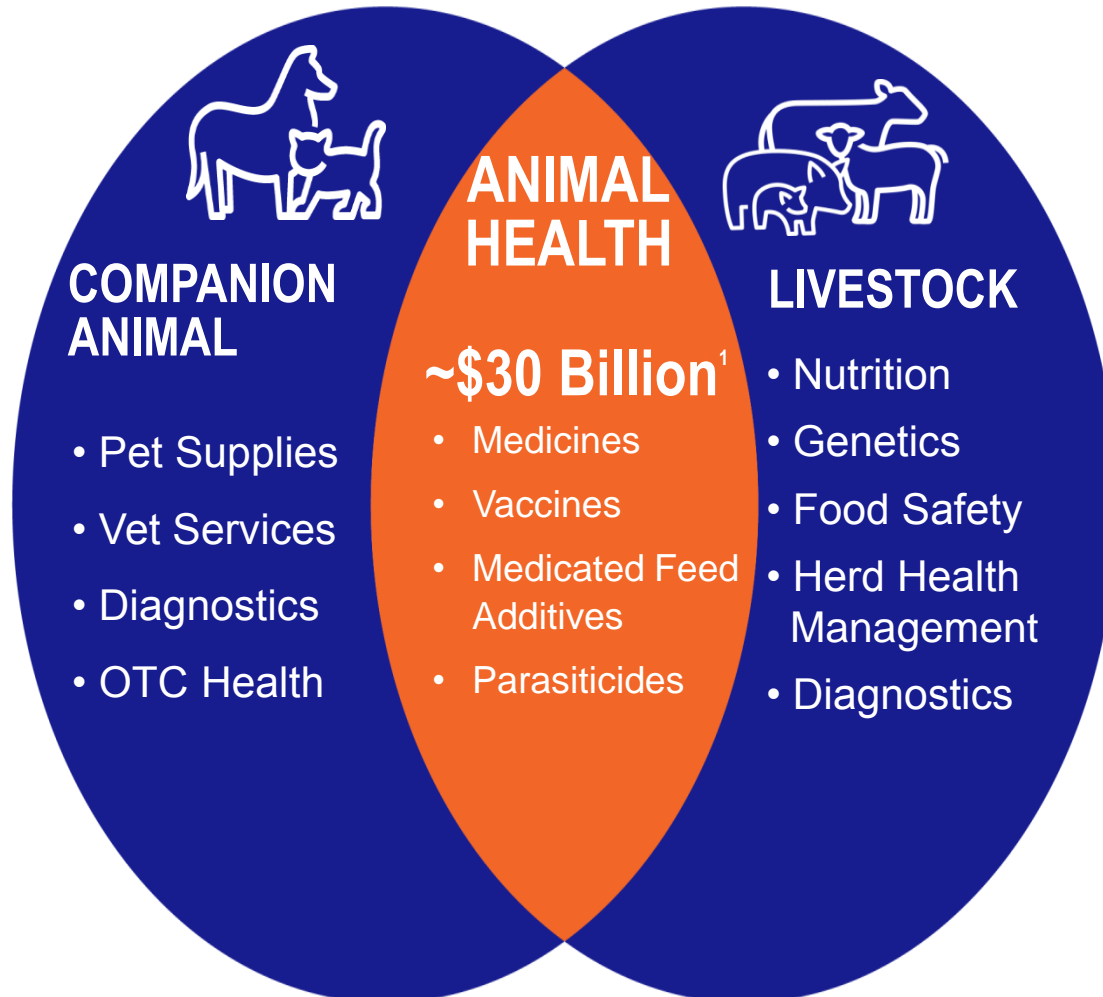
**LIVESTOCK
HEALTH**



**COMPANION
ANIMAL
HEALTH**

AT THE CORE OF A \$100+ BILLION INDUSTRY

~\$30B GLOBAL ANIMAL HEALTH MARKET

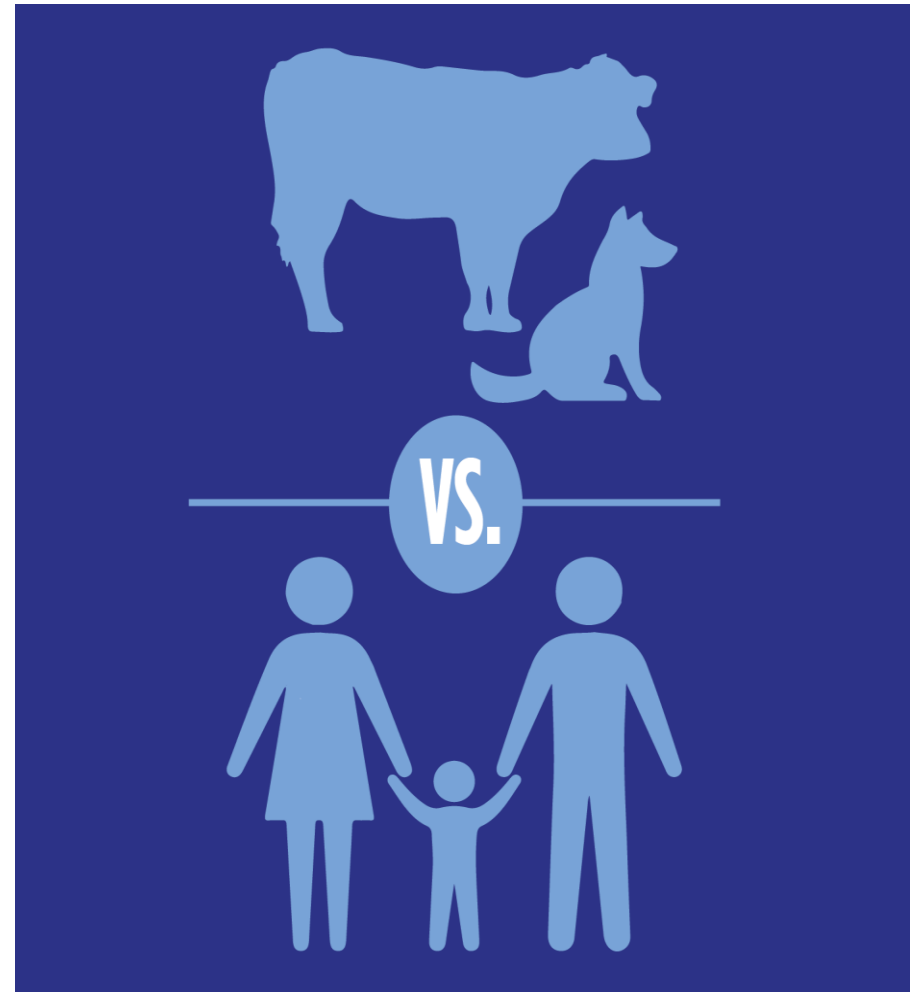


¹ Vetrinosis Review 2015

A DISTINCT INDUSTRY

ANIMAL HEALTH DIFFERS FROM HUMAN HEALTH

- Limited third-party payers; direct selling relationships
- Less generic competition; greater brand loyalty
- Innovation combined with focus on product lifecycle development
- More predictable and less costly R&D model
- Complexity of 8 different species and distinct regional needs



POWERFUL TRENDS CREATING DEMAND

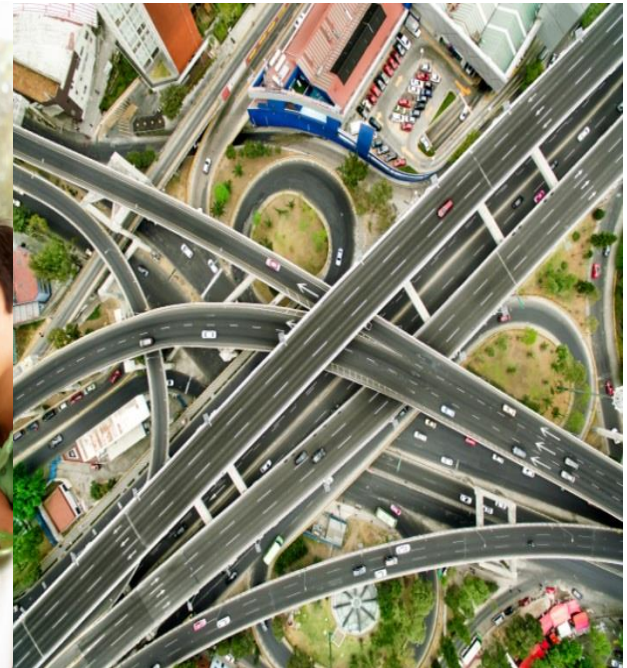
PREDICTABLE, SUSTAINABLE AND FUNDAMENTAL ECONOMIC DRIVERS



**POPULATION
GROWTH**



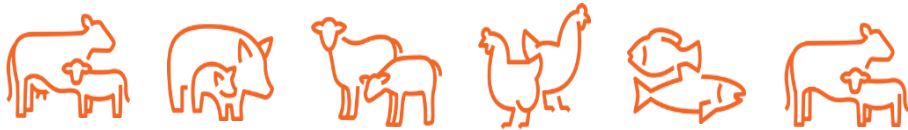
**A GROWING
MIDDLE CLASS**



**INCREASING
URBANIZATION**

KEY DRIVERS OF GROWTH

LIVESTOCK



COMPANION ANIMALS



Global population growth

30% from 1990-2010 ¹

Economic development, particularly in emerging markets

Increased demand for animal protein

Productivity improvements

Increased ownership and medicalization

Unmet medical needs

¹ Source: United Nations

THE WORLD DEPENDS ON ANIMALS

RELYING ON LIVESTOCK FOR NOURISHMENT

7
BILLION

people consume animal protein as milk, meat, poultry, fish and eggs¹



40%

of the global value of agricultural output² is from the livestock sector

33%

of arable land is dedicated to producing feed for livestock³

¹ Euromonitor International ² SOFA Report 2009 ³ FAO-Agriculture and Consumer Protection Department: Livestock's Long Shadow, Environmental Issues and Options, 2007

THE WORLD DEPENDS ON ANIMALS

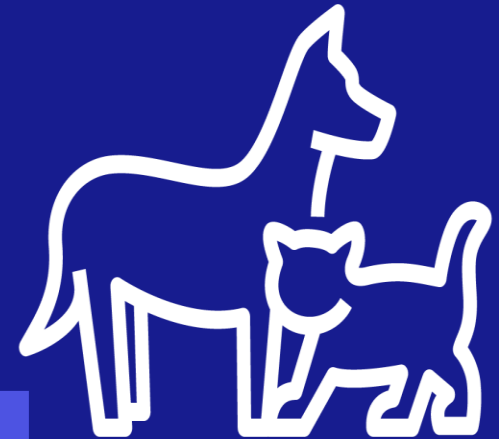
COMPANION ANIMALS ENRICH PEOPLE'S LIVES

350
MILLION

there are more than 225¹ million dogs² and 125¹ million cats² living in homes worldwide

62%

of American households own at least one dog or cat³



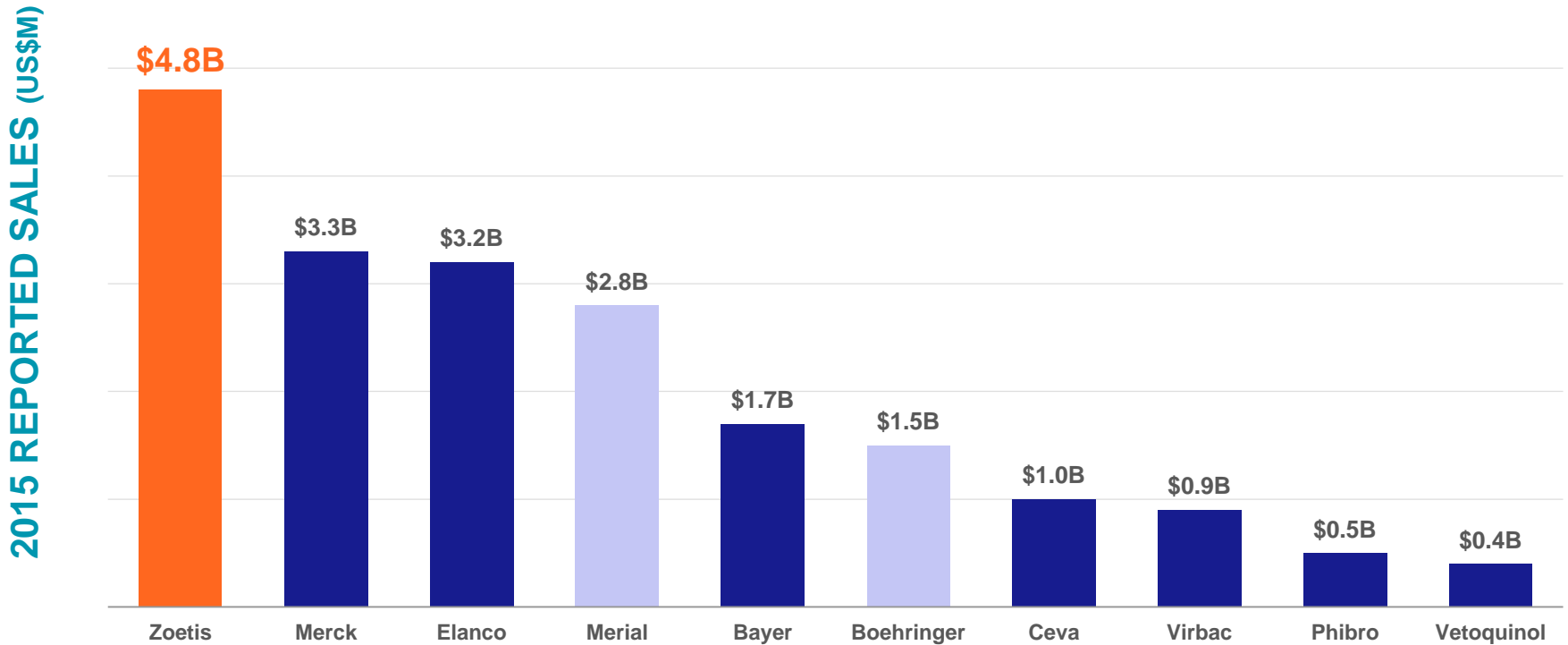
15%

pet spending in Brazil, Russia and China has been growing by more than 15% per year⁴

¹ Vetnosis ² Viewed as medicalized treatable units by Vetnosis ³ 2011-2012 APPA National Pet Owners Survey ⁴ The Freedonia Group

ZOETIS LEADS THE ANIMAL HEALTH INDUSTRY

2015 AH REPORTED SALES (INCLUDING NON-AH SALES)



Source: *Vetnosis Executive's Guide 2016* and public filings for certain companies.

On December 15th, 2015 Sanofi (Merial) and Boehringer announced they had entered exclusive negotiations on a business swap that would make Boehringer the second largest animal health company.



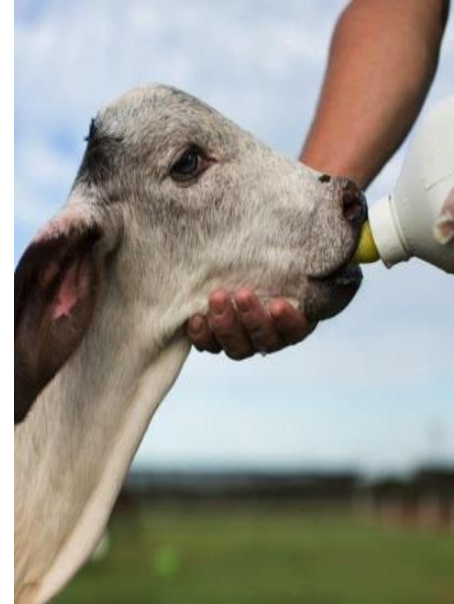
COMPANY OVERVIEW

THE ANIMAL HEALTH INDUSTRY

We support our livestock customers in achieving two key imperatives:

Productivity: By the year 2050, the world will need to double food production to feed our global population.

Food safety: A wholesome and sustainable global food supply keeps the world's population well-nourished.



62%

Our livestock health portfolio represents **62%** of our business revenue with products and services for dairy cattle, beef cattle, sheep, pigs, poultry and fish.¹

¹Based on 2015 revenue. Excludes revenue associated with Client Supply Services (CSS), which represented 1% of total 2015 revenue.

LIVESTOCK HEALTH PORTFOLIO

SELECT PRODUCTS AND SERVICES



Swine



Poultry



Dairy
Cattle



Beef
Cattle



Sheep



Not all products or services shown are approved for use in all regions. Contact Zoetis Legal and Regulatory for additional information.
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COMPANION ANIMAL HEALTH PORTFOLIO

Our companion animal health business strives to provide veterinarians with the resources they need to provide the highest quality of care and support so that companion animals can stay active and well.

Our products can help improve the quality and extend the life of dogs, cats and horses, while also making it easier for owners to guarantee the health and wellness of their companion animals.



37%

Our companion animal health portfolio represents 37% of our business revenue with products and services for dogs, cats and horses.¹

¹Based on 2015 revenue. Excludes revenue associated with Client Supply Services (CSS), which represented 1% of total 2015 revenue.

COMPANION ANIMAL HEALTH PORTFOLIO

SELECT PRODUCTS AND SERVICES



Dogs



Cats



Horses

apoquel[®]

ProHeart[®]
INJECTION

Synulox[™]

convenia[™]

FELOCELL[®]

DORMOSEDAN[®]

QUEST[®]

BRONCHICINE[®]
CAe

revolution[®]

Trocoxil[®]
KOVANOL

Cerenia[™]

revolution[®]

EQUEST[®]

Strongid[®] C 2X

Cerenia[™]

RIMADYL[®]

VANGUARD[®]

CLAVAMOX[®]

stronghold[®]

EXCEDE[®]

West Nile
Innovator[®]

convenia[™]

Sileo[®]

VANGUARD[®] Lyme

DEXDOMITOR[®] D

Synulox[™]

Fluvac
Innovator[®]

Zylexis[®]

CLAVAMOX[®]

Simparica[®]

VERSICAN[®]
Plus

Palladia[®]

stronghold[®]

WITNESS[™]

Not all products or services shown are approved for use in all regions. Contact Zoetis Legal and Regulatory for additional information

Sileo[®] is trademark owned by Orion Corporation Orion Pharma Animal Health. It is manufactured by Orion Corporation and distributed by Zoetis under license from Orion Corporation Orion Pharma Animal Health. DEXDOMITOR[®] and DORMOSEDAN[®] are trademark owned by Orion Corporation and Orion Pharma. They are developed and manufactured by Orion Corporation Orion Pharma Finland and distributed by Zoetis. All trademarks are the property of Zoetis Services LLC or a related company or a licensor unless otherwise noted.

zoetis



We also serve our customers and their businesses with diagnostic and genetic products and services.



OUR COMPLEMENTARY BUSINESSES

Our **diagnostic** products help monitor and safeguard the health of animals.

- Enzyme linked immuno-sorbent assay (ELISA)
- Rapid Immuno Migration (RIM™)
- Agar gel immuno-diffusion (AGID)



Our **genetic** solutions are designed to provide accurate genetic predictions.

- HD 50K for Angus
- CLARIFIDE® Plus for Dairy
- Sheep 50K
- CLARIFIDE® for Nelore



ESTABLISHED PRESENCE IN BOTH DEVELOPED AND EMERGING MARKETS



100+

Countries where our products are sold

TOTAL REVENUE SPLIT¹

77%

Developed markets

23%

Emerging markets



2,800

Member field force in approximately 45 countries

¹Based on 2015 revenue

LEADERSHIP IN PRODUCT DEVELOPMENT

Zoetis is committed to continuously innovating to develop animal health solutions that meet the needs of those who raise and care for animals.

We apply our research to a broad and diverse range of species, therapeutic areas and geographic regions.

OUR AREAS OF FOCUS ARE:

- Medicines
- Vaccines
- Diagnostic Tests
- Genetics
- Biodevices



LEADERSHIP IN PRODUCT LIFECYCLE INNOVATION

R&D is at the core of our efforts to provide innovation outcomes that anticipate the future needs of veterinarians and livestock producers in their local markets around the globe.

NEW PRODUCT DEVELOPMENT

- New chemical entities
- New antigen targets
- New biopharmaceutical approaches to prevent or treat disease
- Integrating research programs for genetics, diagnostics and core product offerings

PRODUCT LIFECYCLE INNOVATION

- Adapting existing approved products for use in new species
- New claims on existing products
- Major reformulations
- New combinations
- Approvals of existing products in new countries
- Market support
- Generic agents



zoetis

LEADERSHIP IN ALLIANCES

STRATEGIC PARTNERSHIPS

STRATEGIC PARTNERSHIPS

Our team is comprised of animal health, scientific and business experts who collaborate with external R&D partners and institutions. Together, we explore new market opportunities, technology and product acquisitions.

THREE KEY AREAS OF FOCUS

- Developing research collaborations and networks around the world
- New research models through participation in consortia with experts
- Identification and rapid response to emerging infectious diseases and collaborative food safety initiatives

GLOBAL ALLIANCE INITIATIVES



HIGH-QUALITY PRODUCTS, DELIVERED BY OUR WORLD-CLASS MANUFACTURING OPERATIONS



**EXCELLENCE
IN QUALITY**



**BREADTH OF
EXPERTISE**



**RELIABLE
SUPPLY**



**SPEED TO
MARKET**

**COST/EFFICIENCY
IMPROVEMENTS**



¹ This site is operated by the Jilin Zoetis Guoyuan Animal Health Co, Ltd., joint venture
NOTE: Sites shown are as of April 2016.



HOW WE DELIVER VALUE

COMPETITIVE ADVANTAGE

THREE INTERCONNECTED CAPABILITIES UNDERPIN BUSINESS MODEL



DIRECT SALES



INNOVATION



HIGH-QUALITY
PRODUCTS

ENHANCING OUR LONG-TERM VALUE PROPOSITION WITH BUSINESS DEVELOPMENT

APPLYING DISCIPLINED PORTFOLIO MANAGEMENT FOR GROWTH

BUSINESS DEVELOPMENT STRENGTHS AND EXPERIENCE

Position of Strength: Core Capabilities and Scale
Experienced in Licensing, Acquisitions, Integrations & Divestitures
Partner of Choice for Animal Health Community

AREAS OF FOCUS

- **Support for R&D Portfolio**
New chemical entities, biological substrates and technologies
- **Complementary Areas**
BioDevices, Diagnostics, Food Safety
- **Portfolio Gaps & Geographical Opportunities**

ASSESSMENT CRITERIA

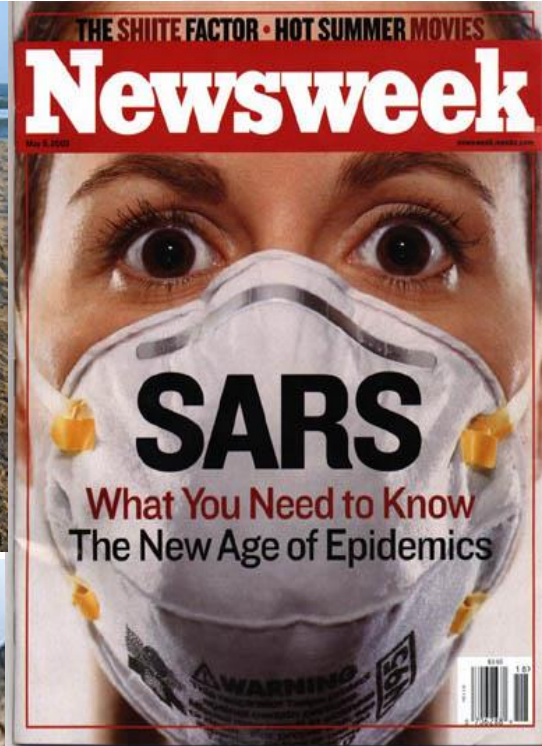
- **Strategic Fit**
- **Clear Synergies**
- **Financial Value**
- **Anti-trust Considerations**

zoetis

www.zoetis.com

One Health Research at the School of Veterinary Medicine

Dan Horton & Martha Betson



Food security

- By 2050 we will have to feed 9 billion people, increasing demand for animal protein

Disease emergence

- A new disease emerges every 3 months, 70% zoonoses

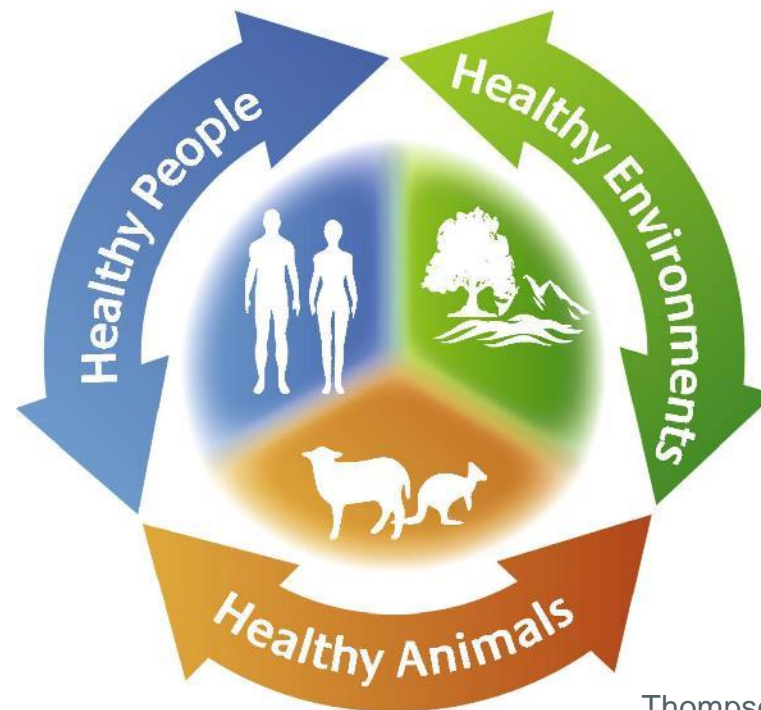
Antimicrobial resistance

- No new antimicrobials since the 1980's, new multi-drug resistant bacterial strains

Epidemics

- A more connected with higher densities of people & animals, accidental or deliberate release of epidemic pathogens

The One Health Triad



Thompson (2014) Int J Parasitol 43:1079

William Karesh, DVM

"Human or livestock or wildlife health can't be discussed in isolation anymore. There is just one health."



Pathology and
digital pathology

Oncology &
neurology



Endocrinology

Antimicrobial
resistance

Physiology



Molecular
epidemiology



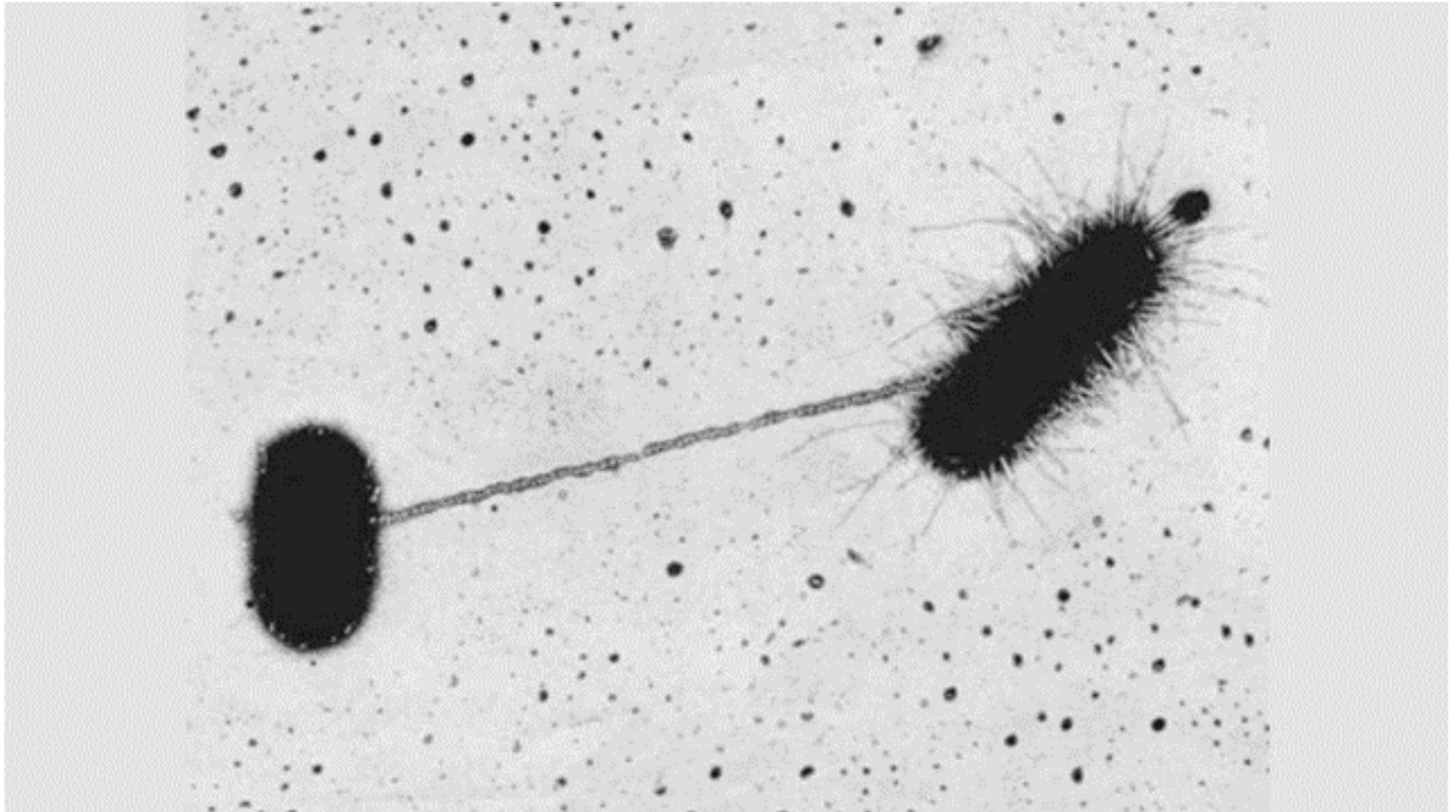
Metagenomics &
microbiome



Diagnostic test
development

Antimicrobial resistance

Mobile Genetic Elements



Antimicrobial resistance

Research at the School of Veterinary Medicine

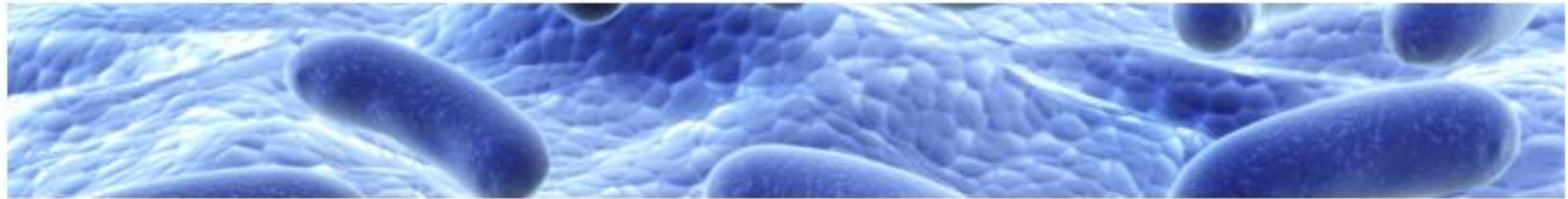
- Understanding how antibiotic resistance is spread from one bacterium to another in hosts or in the environment
- Investigating how antibiotic resistance can contribute to how bacteria cause disease in animals and humans
- Understanding how bacteria develop antimicrobial resistance
- Developing alternatives to antibiotics for use in animals and humans
- Developing rapid diagnostics to detect antibiotic resistance

Freire Martin *et al* 2014, Szych *et al* 2014, Mappley *et al* 2013



Antimicrobial resistance

Cross disciplinary working:



COLLABORATIVE HUB FOR ADVANCING INTERDISCIPLINARY RESEARCH

The aim of the Collaborative Hub for Advancing Interdisciplinary Research (CHAIR) is to create and support networks of researchers who together will develop a strong collaborative community. The focus is on developing novel strategies to detect and mitigate the emergence of antimicrobial resistance (AMR) in zoonotic pathogens. This should lead to exciting funding opportunities for engineering and physical scientists.



Engineering and Physical Sciences
Research Council

New rapid diagnostics- why?

- Culture and sensitivity tests can take up to 5 days
- Samples have to be sent off to private laboratories
- Expensive

Lack of testing



inappropriate antibiotic usage



Antimicrobial resistance

- Welfare
- Economics

New rapid diagnostics

- Based on LAMP (loop-mediated isothermal amplification) technology
- Allows rapid pen-side or point-of-care testing
- Already developed: *Staphylococcus pseudintermedius*

Diribe *et al* 2014,
Diribe *et al* 2015



New rapid diagnostics

Food borne diseases (*Hepatitis E virus*)



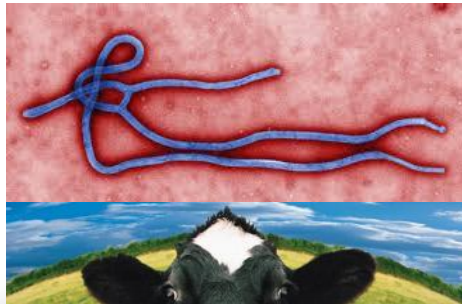
Parasitic diseases (*Ascaris*)



Neglected zoonoses (*Rabies*)



Identifying novel viruses



- Rapid detection of emerging pathogens is essential to mitigate their impact
- Technology for virus detection using next generation sequencing is available
- Not adequately optimised

OPEN ACCESS Freely available online

PLOS | PATHOGENS

Pearls

A Roadmap to the Human Virome

Eric Delwart^{1,2*}

1 Blood Systems Research Institute, San Francisco, California, United States of America, 2 Department of Laboratory Medicine, University of California at San Francisco, San Francisco, California, United States of America



↓
VIROME in
bushmeat and
domestic animal
samples

Lumley *et al* 2016

What is the reservoir?

Where is the reservoir?

Diqqət! Diqqət! Diqqət!



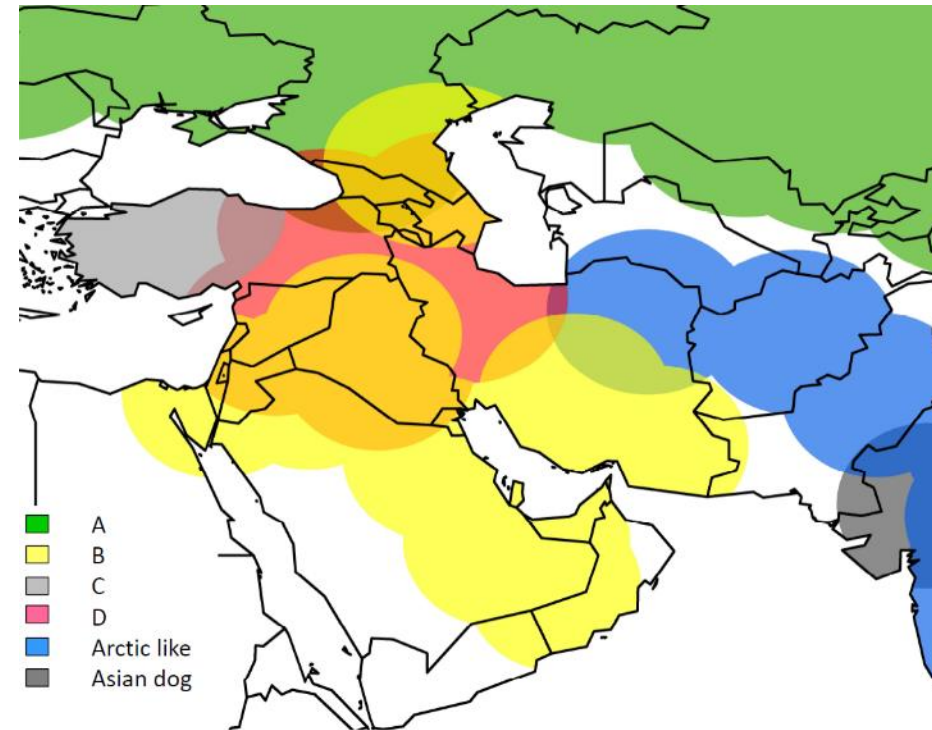
QUDUZLUĞUN ƏLAMƏTLƏRİ:
AĞIZIN SULANMASI,
AQRƏSSİVLİK VƏ YA
SAKİTLİK, ANORMAL
DAVRANIŞ

ƏGƏR SİZ QUDUZLUQDAN
ŞÜBHƏLƏNİRSİNİZSƏ,
DƏRHAL SAHƏ BAYTAR
HƏKİMİ VƏ YA RAYON
BAYTARLIQ İDARƏSİNƏ
XƏBƏR VERİN



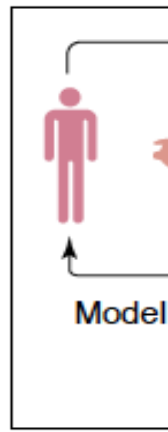
QUDUZLUQUN
QIZIL QANLI XƏSTƏLİLİYİ
10-1115 - ƏSAS QIZIL
SƏHİBƏSİ, 3122 SƏHİBƏ
Tel: 994 12 92716 57 Fax: 994 12 562 06 32

DBS-nin QAYNAR İQTİD: 603 0006

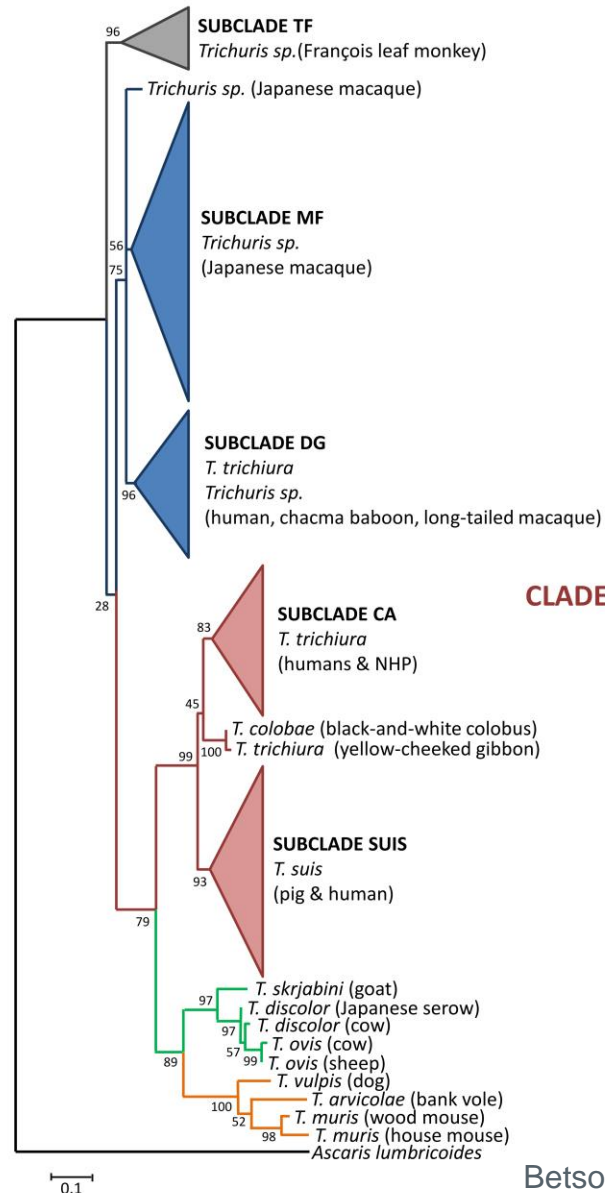


Horton *et al* 2015

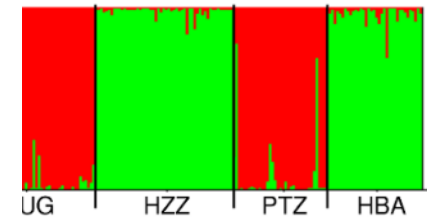
Tracking parasite transmission



Anderson

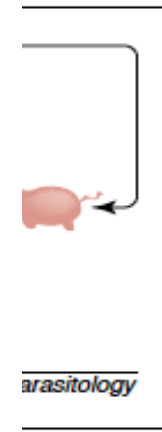


CLADE 2



Betson *et al* 2014

CLADE 1-CPGOB



CLADE 3

CLADE 4

Betson *et al* 2016



Acknowledgments

Roberto La Ragione

Alasdair Cook

Chris Stevens

Clare Rusbridge

Javier Salguero Bodes



The Royal Veterinary College

More than just a school of veterinary medicine

Mandy Nevel BSc BVetMed PhD FHEA MRCVS

Bevan McWilliam – Business Relationship Manager

bmcwilliam@rvc.ac.uk

+44 (0)20 3214 8127

www.rvc.com

The Royal Veterinary College

➤ First English-speaking vet school

- 1792, first students
- Today, 1600 students
- 47 Nationalities
- High retention rates
- High standards



➤ Campuses in Camden and Potters Bar, Hertfordshire

➤ Working farm

➤ Veterinary & Biomedical focus



Learning at the RVC

- 12 undergraduate and Masters programmes
 - Veterinary Medicine, Science & Nursing (1,800 students)
 - Veterinary Continuing Professional Development
 - Epidemiology, Wild Animal Biology, Pathology
- 130 PhD studentships in basic, translational and clinical research



World leading Hospitals

- ▼ The College's small and large animal hospitals treat over 20,000 patients each year.
- ▼ Queen Mother Hospital for Animals (referral)
 - Europe's leading small animal hospital
 - Centre of excellence for a large veterinary pharmaceutical company
- ▼ Beaumont Hospital (1st opinion)
- ▼ Equine Referral Hospital
- ▼ Farm Animal Practice
- ▼ Diagnostic Laboratory



Translational Medicine

- Queen Mother Hospital is centre of excellence for a large veterinary pharmaceutical company
- Interest in expediting the drug discovery process to phase IIb
- Large cross over between animal and human diseases e.g. type II diabetes, obesity, chronic pain
- Growing strengths in cell therapy



Research at the RVC

- Comparative Biomedical Sciences
 - biomechanics, musculoskeletal biology, cardiovascular biology, reproduction, development and pharmacology
- Clinical Sciences and Services
 - clinical services division, centre for veterinary nursing, clinical investigations centre, CPD
- Pathogen and Pathogen Biology
 - viruses (BVDV, canine respiratory), bacteriology (mycoplasmas), parasite biology and vaccine development
- Production and Population Health
 - veterinary epidemiology, economics and public health group; centre for animal welfare, farm health & production



Centre for Emerging, Endemic and Exotic Diseases (CEEED)

Through the VEEPH the RVC was recognised in 2012 as a United Nations Food and Agriculture Organisation Reference Centre for Veterinary Epidemiology.

RVC Business

- Support for any bioveterinary or biomedical company looking to develop innovative products and services
 - Provides a quality contract research service
 - Pre-clinical services for drug and medical device development
 - Access to academic expertise of international standing

Small Animal Facilities

- Rats, mice, ferrets
- Companion animals

Large Animal Facilities

- Production animals
- Surgery
- Imaging
 - CT Scanning, Radiography, Scintigraphy, MRI

Our Capabilities

- Our study manager will help you devise and run your study or service, and report on the outcome

STUDIES INCLUDE	SERVICES INCLUDE
Pre-clinical Safety Studies	Medical device testing
Residue Studies	Antisera production
Efficacy Studies	Biological products
PK-PD Modelling	Research services
Models of infectious, cancer, cardiology and orthopaedic disease	Bespoke model development
Parasitology studies	
Animal behaviour, nutrition studies	

- Highest standards of animal care. All projects are reviewed by the Animal Welfare and Ethical Review Board

Facilities

➤ Animal Facilities are located at *both* our campuses

HAWKSHEAD	CAMDEN
Small animal facilities	Small animal facilities
Companion animals	Surgery
Large animal facilities	Quarantine
Surgery	Isolator suite
- CT Scanning	Transgenic breeding
- Radiography	
- Scintigraphy	
- MRI	

- Established contacts with a number of farms for on-farm studies



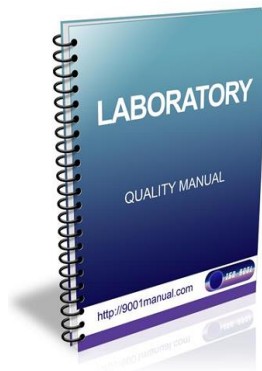


Animal Welfare Barn



Contract Research

- A quality service to biotechnology, nutrition and pharmaceutical companies
- Work to Good Clinical Practice (Veterinary) (GCP(V))
 - We have experience of running GCP(V) studies on farms and are in contact with a number of farms which are suitable for running a variety of studies



What we do

- Support for Working with Industry
- Intellectual Property Protection
- Contracts / Agreements Negotiation
- Staff and Student Enterprise Training
- Managing and Marketing the LBIC



More than Just Veterinary Medicine

- Leading veterinary educational provider
- Research intensive with animal, translational and human health interests
- Highly collaborative – aim to be a great partner





The UK Pig Industry – Opportunities and Issues

Mandy Nevel

Outline

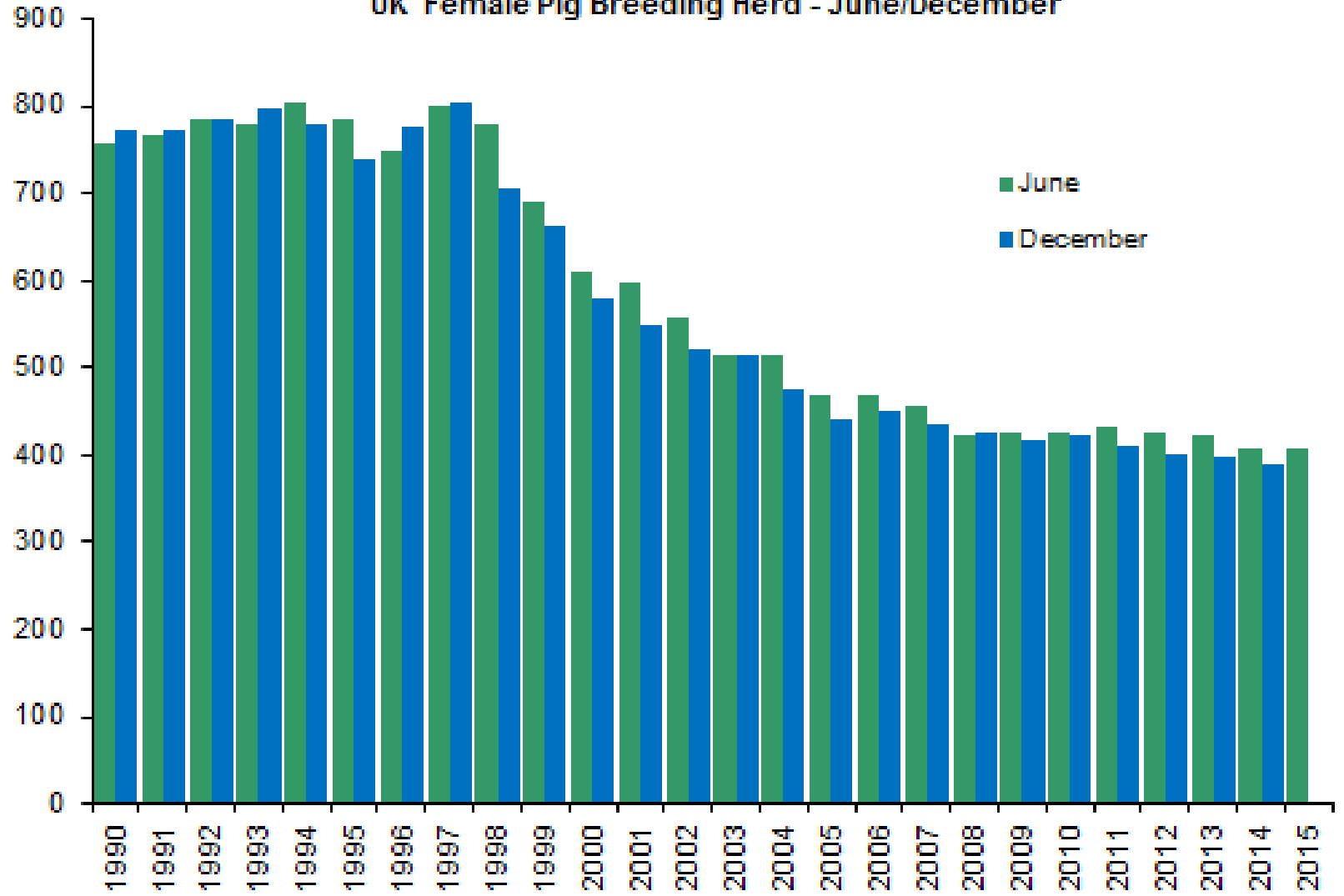
1. Industry structure
2. Opportunities
3. Issues
4. The future

1. The UK industry

- Small, unique industry
 - 410,000 sows, 50% housed outdoors
 - Producing about 28p/s/y
 - Loose housed and later weaning (28 days)
 - Do not castrate (93%)
 - Slaughter at 90kg

000 head

UK Female Pig Breeding Herd - June/December



Source AHDB Pork

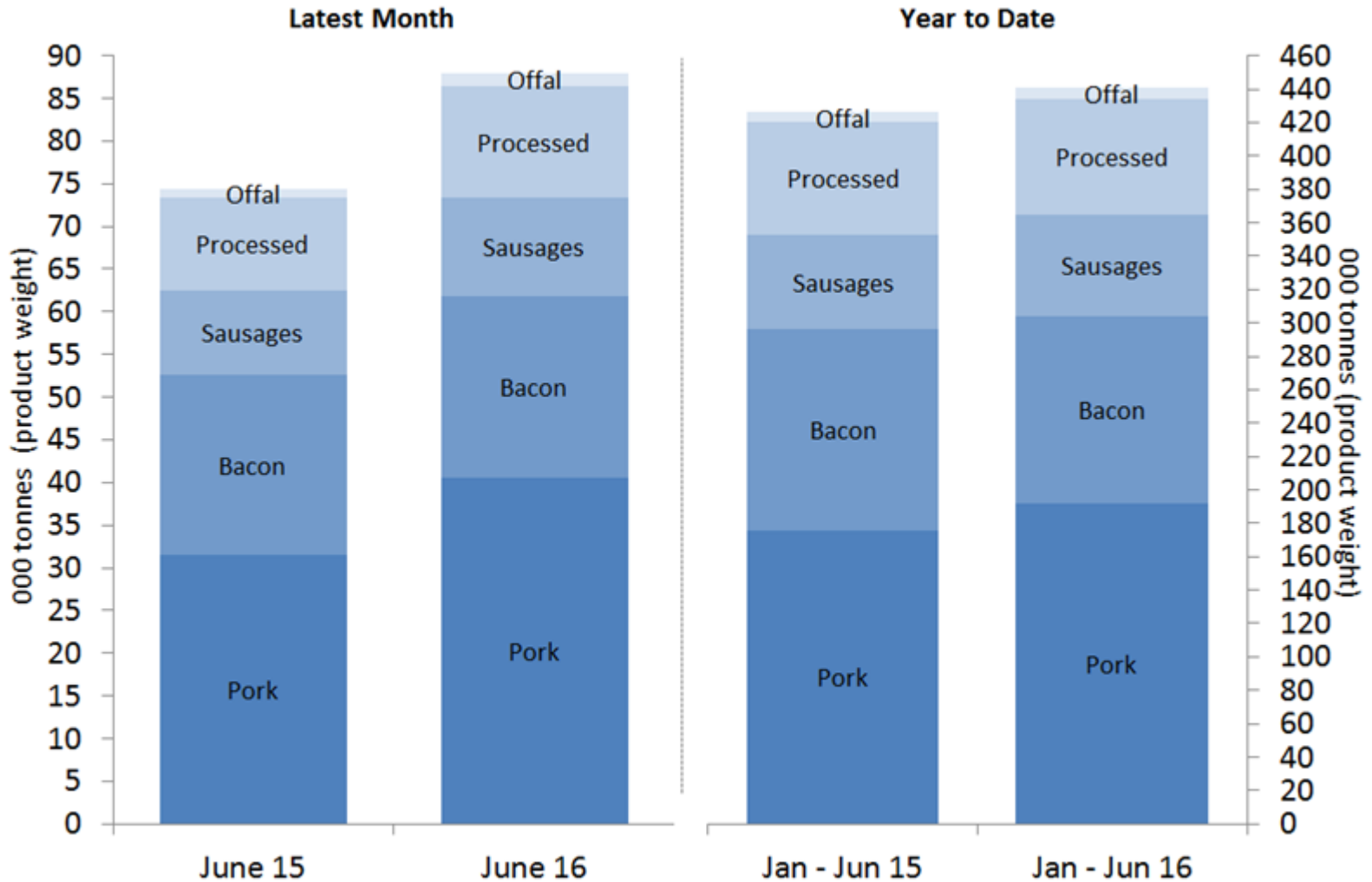
Outdoor pigs





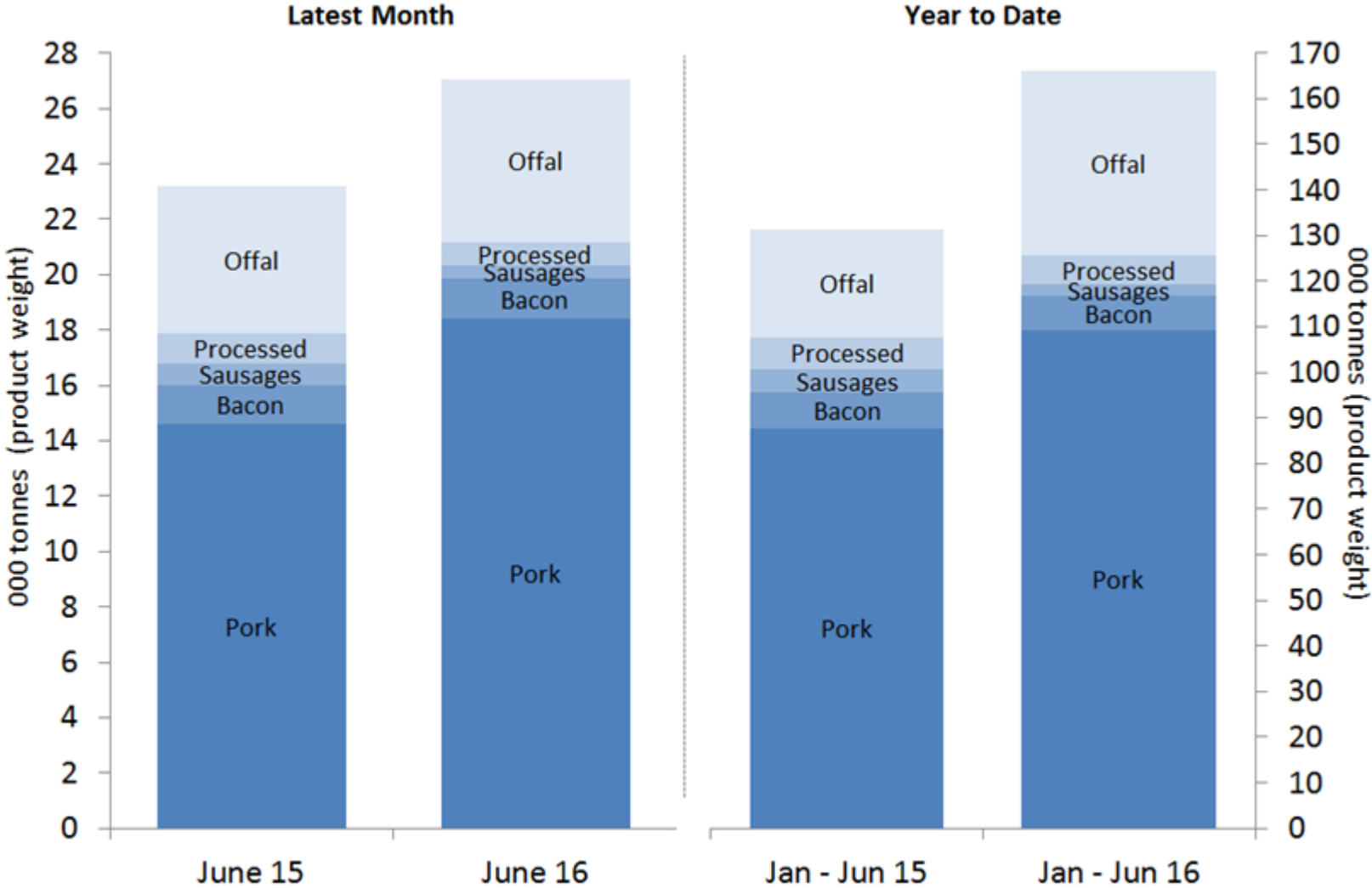


UK Pig Meat Imports



Source: Her Majesty's Revenue & Customs

UK Pig Meat Exports



Source: Her Majesty's Revenue & Customs

Small but significant smallholder



And wild boar



2. Opportunities

- To keep disease out
- To develop better/bespoke vaccines
- Education
- Genetics
- Nutrition
- (Welfare)

3. Issues

- AMR
- Advancing ASF
- PEDv
- **Endemic Disease**
- HP PRRS
- Lack of investment in buildings
- (Welfare)

Endemic disease

- *Mycoplasma hyopneumonia*
- *Actinobacillus pleuropneumoniae*
- PRRS
- PCV2

Abattoir surveillance



Oral Fluids



4. The Future

- Better vaccines
- Better genetics
- Improved health
- Better nutrition
- Improved diagnostics

Questions





altimmune

Gaithersburg – London – Strasbourg

**Immunotherapeutic vaccines for
respiratory infections, chronic
viral infections and cancer**

September 2016

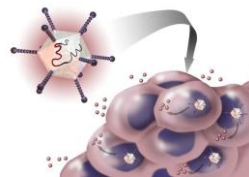
**Katie Anderson PhD
Pre-clinical and Analytical Project Manager
Altimune UK**

Proprietary Platform Technologies

Two distinct, complementary vaccine platform technologies activate the immune system in different ways to traditional vaccines

RespirVec

- Replication-deficient adenovirus delivered intranasally to upper respiratory tract
- Inserted transgenes encode infectious disease viral proteins
 - Broad activation of the immune system
 - Bypasses pre-existing and anti-vector immunity
 - Self-adjuvanting with the potential to improve immunogenicity
 - Rapid production cycle



Densigen

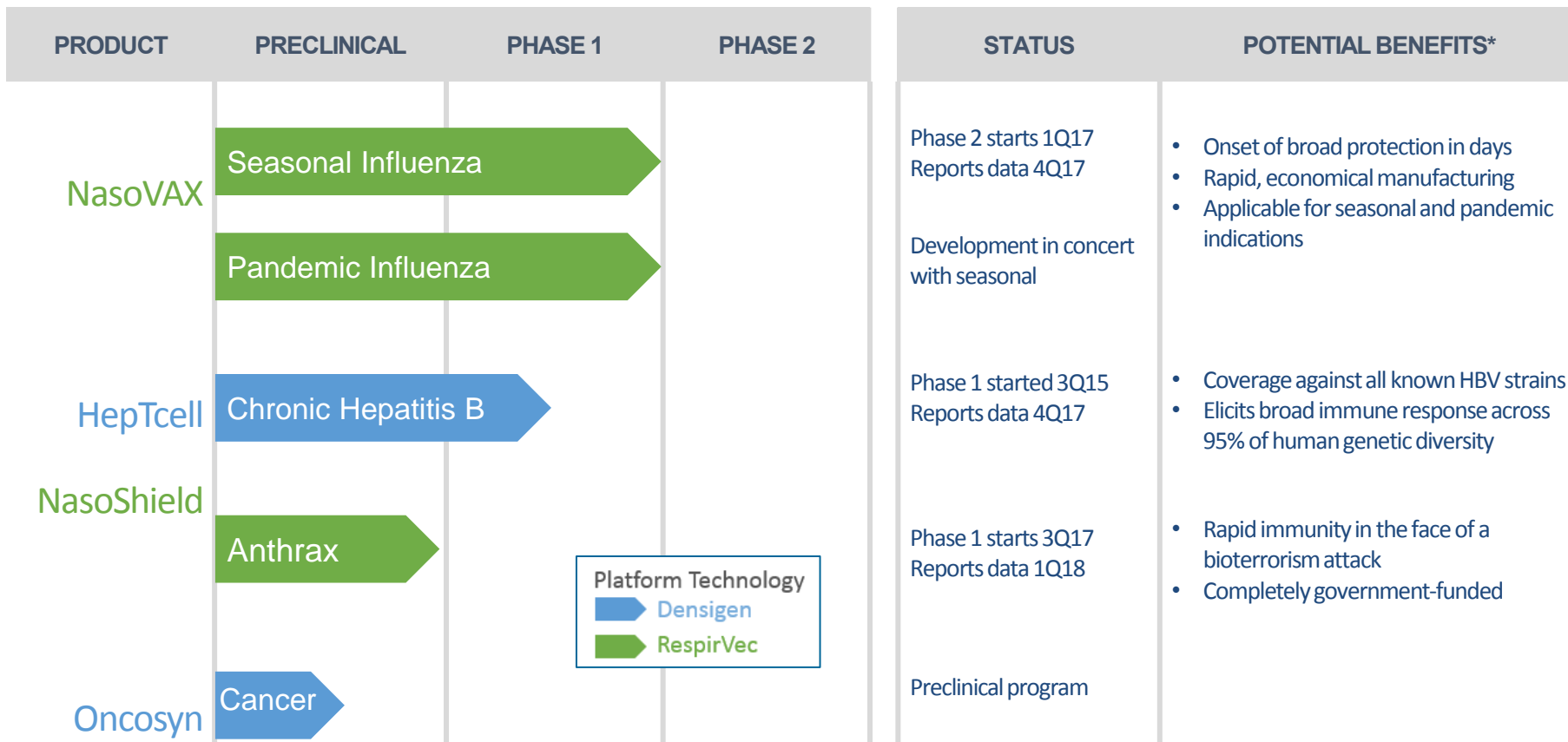
- Stable, synthetic peptide immunotherapeutic platform:
 - T cell-directed approach, without HLA restriction
 - Innovative peptide modification improves immunogenicity
 - Targets multiple pathogens simultaneously
 - Activation of diseased cell killing by T cells



Product Pipeline



Novel product candidates utilizing a new approach to engage the immune system, offering fundamental advantages over competing therapies



Multiple near-term clinical milestones

*Based on observations in preclinical and early clinical trials. Preclinical and clinical results are not necessarily predictive of the final results of ongoing or future clinical trials.

Human Immune System



Innate Immune Response

- Initiates *immediately* to recognise invading viruses, bacteria, and fungi
- Protects against infection while adaptive immune response develops

Adaptive Immune Response

- Highly specific, developed over extended period of time
 - **Antibody-Mediated Humoral Immunity:** neutralisation of extracellular pathogens, such as viruses
 - **T cell-Mediated Cellular Immunity:** recognises cancer cells and cells harboring pathogens that need to be destroyed
 - **Mucosal Immunity:** localised to mucosal tissues and utilizes IgA (specialized antibody) to destroy pathogens at site of entry

HepTcell for Chronic Hepatitis B



Market

- 350 million people chronically infected worldwide with >1 million HBV-related deaths/year⁶
- ~\$3 billion global chronic hepatitis B market⁷

Key Differentiators

- Uses Densigen technology
- T cell activating approach: potential for disease cure
- Viral targets chosen to elicit broad HLA type-independent immune responses
- Targets all known strains of HBV: increased efficacy

Upcoming Milestones

- Phase 1 started 2Q15, data expected 4Q17

⁶Hepatitis B Foundation

⁷Hepatitis B Therapeutics in Major Developed Markets to 2021, GBI Research, Sep. 2015 ²²⁵

HepTcell: therapeutic vaccine to treat chronic HBV



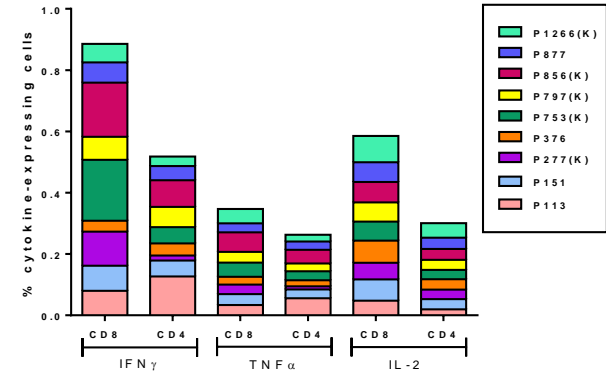
altimmune

- Nine 32-40mer synthetic peptides, each conjugated to a fluorocarbon moiety which provides self-adjuvanting properties.
- Sequences derived from conserved regions of HBV proteome: polymerase, core, surface proteins.
- Contains multiple CD4+ and CD8+ T cell epitopes; bypasses HLA restriction providing broad population coverage.
- Targets multiple HBV genotypes, elicits immune responses across subject ethnicities.



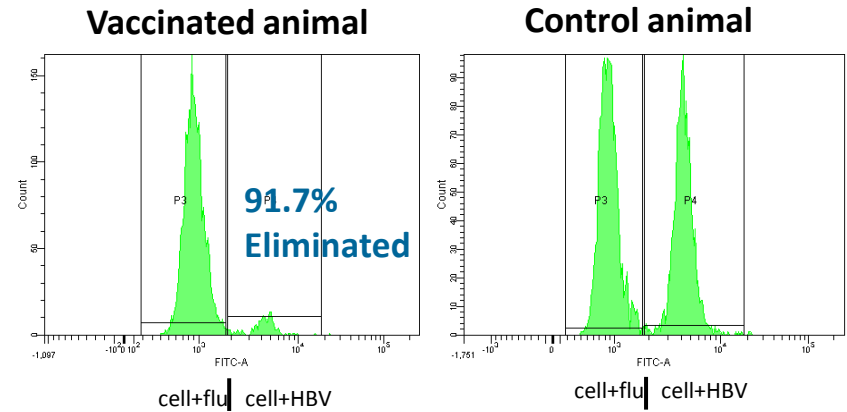
HepTcell: Pre-clinical Data

Elicits CD4+ and CD8+ polyfunctional T cell responses (anti-viral cytokines) in PBMC from chronic HBV subjects.



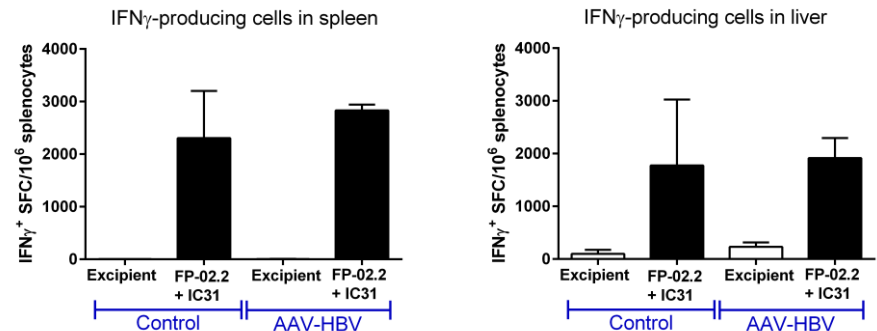
Induces expansion of functional killer T cells in vivo.

- Mouse 'target' cells loaded with HBV proteins or unrelated viral proteins injected into mice vaccinated with HepTcell (1:1 ratio)
- Within 1 day, 92% of HBV-loaded cells were eliminated



Surmounts HBV-induced immune tolerance

- Immunised mice generated robust T cell response in presence of HBV infection



HepTcell: Clinical Development



PHASE 1

- **Double-blinded, placebo-controlled trial in 72 patients**
 - Chronic Hepatitis B disease population controlled with nucleos(t)ide therapy
- 3 cohorts (n = 18, 36, 18); receive HepTcell at days 1, 29, and 57
 - Low vs high dose HepTcell ± IC31 adjuvant
 - Controlled for placebo and IC31 effects
- **Study Objectives**
 - Primary: Assess safety and tolerability
 - Secondary: T cell response, HBsAg and HBsAg-antibody levels, assess phenotype of cell-mediated immune response
- Data available 4Q2017

PHASE 2

- Expanded study in Asia/Pacific and US in 1H2018
- Schedule may be re-evaluated based on Phase 1 data
- Anticipate 120 – 200 patients

Single-dose intranasal influenza vaccine delivered using the RespirVec platform

- Potential significant advantages over traditional flu vaccines:
 - Cross-protection against changing virus strains
 - Rapid protection (days rather than weeks)
 - Indicated in young children, adults >65, pregnant women and people with underlying medical conditions
 - Mucosal immunity at site of infection
 - Immune activation at very low doses
 - >50% reduction in production time and at anticipated lower costs compared to traditional egg-based manufacture

Based on observations in preclinical and early clinical trials. Preclinical and clinical results are not necessarily predictive of the final results of our ongoing or future clinical trials.

NasoVAX: Phase 2 Clinical Development



<p>PART 1: CHALLENGE STUDY</p>	<p>Expected to commence in 1Q17</p> <ul style="list-style-type: none">• 2 treatment arms of 24 patients, each with own placebo control group• Both arms will receive monovalent NasoVAX vaccine matched to challenge strain• <u>Arm A</u>: challenged within a few days to assess rapidity of immunity onset• <u>Arm B</u>: challenged after one month to assess efficacy <p>Data expected in 4Q17</p>
<p>PART 2: DOSE RANGING TRIAL</p>	<p>Expected to commence in 1H18</p> <ul style="list-style-type: none">• 3 cohorts of 50 healthy adults 18-64 yrs will receive quadrivalent NasoVAX• Antibody response and other measures of immunogenicity assessed one month post-vaccination <p>Immunogenicity data 6 months following first enrollment</p>
<p>PART 3: DOSE CONFIRMATION STUDY</p>	<p>Expected to commence in 2018</p> <ul style="list-style-type: none">• 540 subjects, including a small cohort of elderly patients• Assess potential added benefit in sub-population with poor immune response

NasoShield Vaccine for Anthrax



The U.S. Government seeks a faster-acting, safer and more convenient anthrax vaccine

Opportunity

- BioThrax[®] (Anthrax Vaccine Adsorbed) is only anthrax vaccine with FDA approval
 - \$250 million in sales in 2014⁸
- Important limitations include
 - Protection requires 6 months and 3 injections⁹
 - Injection site local adverse reactions in 60-80% of subjects⁹

NasoShield is a well-differentiated anthrax vaccine

- Uses RespirVec technology
- Intranasal administration and faster onset of protection
- Well-tolerated
- Program entirely funded by BARDA

Oncosyn Immunotherapeutic for Cancer



Market

- \$139 billion global market for immuno-oncology by 2021¹⁰

Key Differentiators

- Direct activation of cytotoxic T cells to recognize and kill cancer cells
- Proprietary peptide modification boosts immunogenicity
- Synthetic, off-the-shelf therapy bypasses patient-specific approach
- Potential for use with checkpoint inhibitors and other immunomodulators
- T cell immunotherapy offers potential for disease cure

Upcoming Milestones

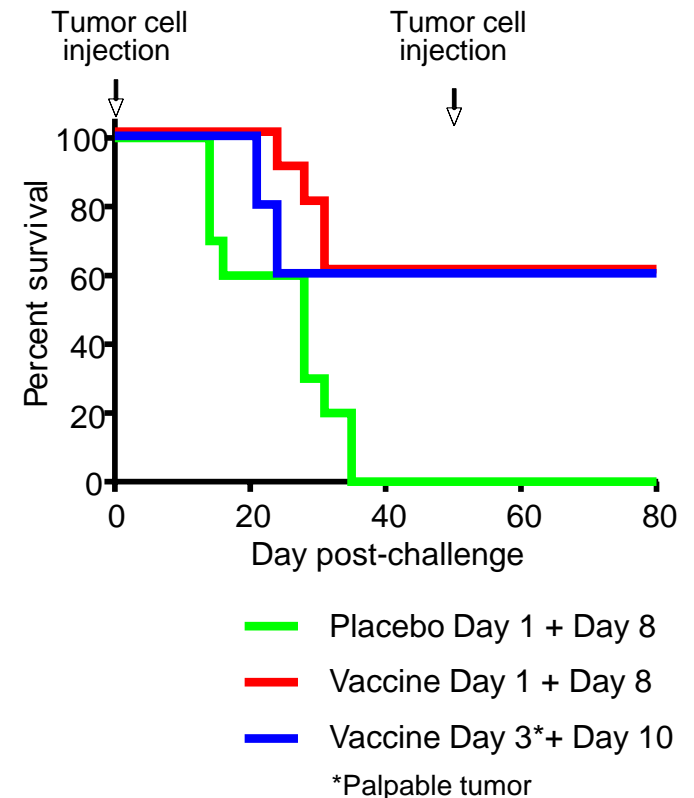
- Preclinical proof-of-concept expected in 4Q16

¹⁰<http://www.prnewswire.com/news-releases/global-immunotherapeutic-market-forecasts-to-2021-for-the-138-billion-industry-300182044.html>

Immunotherapy targeting solid tumors

- Densigen platform technology activates immune response against a tumor
- Activity in mouse model tumor system
 - 60% of treated mice survived vs. none of untreated mice
 - Blocked subsequent tumor formation
- Ongoing preclinical studies focusing on:
 - Tumor-associated antigens
 - Ability of immunomodulators to boost Oncosyn's antitumor efficacy

Antitumor activity of tumor-targeted Densigen-based vaccine



Leadership Team



Bill Enright, MA, MS
President & CEO



Bertrand Georges, PhD
Chief Technology Officer



Elizabeth Czerepak, MBA
Chief Financial Officer



Jeff Carey
Sr. Director Regulatory



Scot Roberts, PhD
Chief Scientific Officer



Sybil Tasker, M.D.
Sr. VP, Clinical R&D





Benchmark
Animal Health



Benchmark
Vaccines Ltd

Vaccines for Animal Health

BVL Overview and
capabilities'
Bob Long
Date April 2016





Contents

- Brief history
- Locations
- Introduction to Business
- Flexible manufacturing technology
- Manufacturing network developments
- Technology
- Quality
- People
- Conclusion
- Back up slides





Brief History

- ❖ The business been situated in Braintree since 1977- focussing mainly on poultry diagnostic testing.
- ❖ It grew into a GMP contract vaccine manufacturing company as Mycofarm Ltd and later as part of Grampian Pharmaceuticals.
- ❖ Moved to Warner Drive site in 1988.
- ❖ Acquired by 3i group in 1997 (called Vericore Ltd).
- ❖ Acquired by Novartis Animal Health in 2000.
- ❖ Acquired by Benchmark September 2012 with all staff retained as part of Benchmark Vaccines Ltd.



BVL locations



BVL Braintree

**BVL
Biocampus
(in
Development)**



Benchmark
Vaccines Ltd

BVL Introduction

Business key facts



- What is BVL -BVL is a UK based ***animal health vaccine manufacturing business***
- Core expertise - ***manufacturing vaccines for a broad range of species*** and ***process development***
- Capabilities – ***most technology platforms*** for bacterial, viral, fungal and recombinant antigens
- People- over ***50% of staff are life sciences graduates*** and have huge experience in vaccines technology.



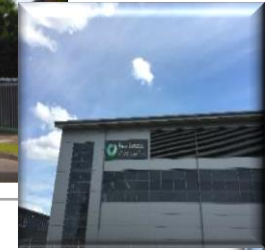
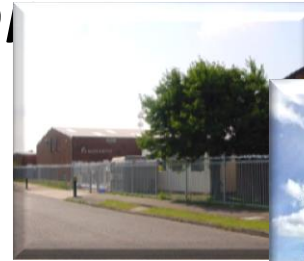
Benchmark Animal Health



Benchmark
Vaccines Ltd

BVL Introduction

Business key facts



- Specialisms - ***Aqua vaccines technology***
- Manufacturing base – ***Braintree, Essex***
- Current customers - ***Animal health divisions of major global pharma companies and Internally BAH***
- New customers - ***Currently negotiating new contracts with a number of Pharma customers***
- Quality- operates to - ***EU GMP and ICH Q10 guidelines***





Key front end services

- Technical transfer of production from donor site or customer R&D
- Process development and validation.
- Test development and validation
- Process problem resolution
- Licensing support

Antigen production platforms

- Roller bottle monolayers –virus production
- Cell Factories monolayer-virus production
- Cell Bioreactors –virus production
- Bacterial fermentation
- Recombinant production
- Fungal culture



Final Product presentations

- Inactivated aqueous formulations
- Inactivated oil emulsions
- Live freeze dried formulations
- Multiple vial size fills
- High volume infusion bags fills
- Plastics multidose pack fills

Finishing

- Full QC testing
- Product labelling and packaging
- QP Release to market
- Global logistics cold chain
- Post marketing stability testing
- Non EU product import and release



Manufacturing Network Development Proj



BVL Braintree facility Biotechnology Building (under development - computer rendering pictures)



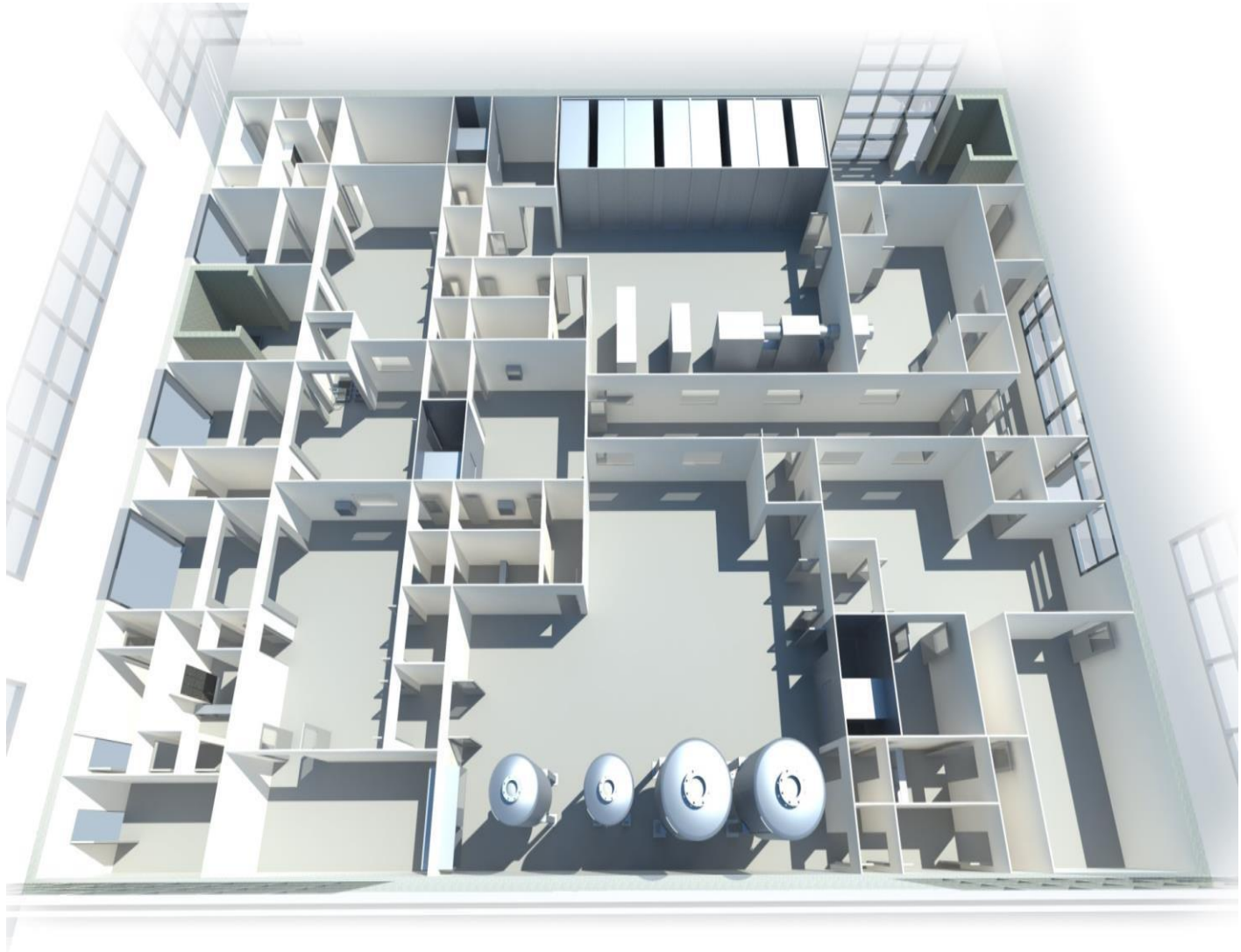
BVL Braintree Biotechnology Building

Completion due September 2016
(Approaching completion)





BVL Braintree facility Biotechnology Building (under development)



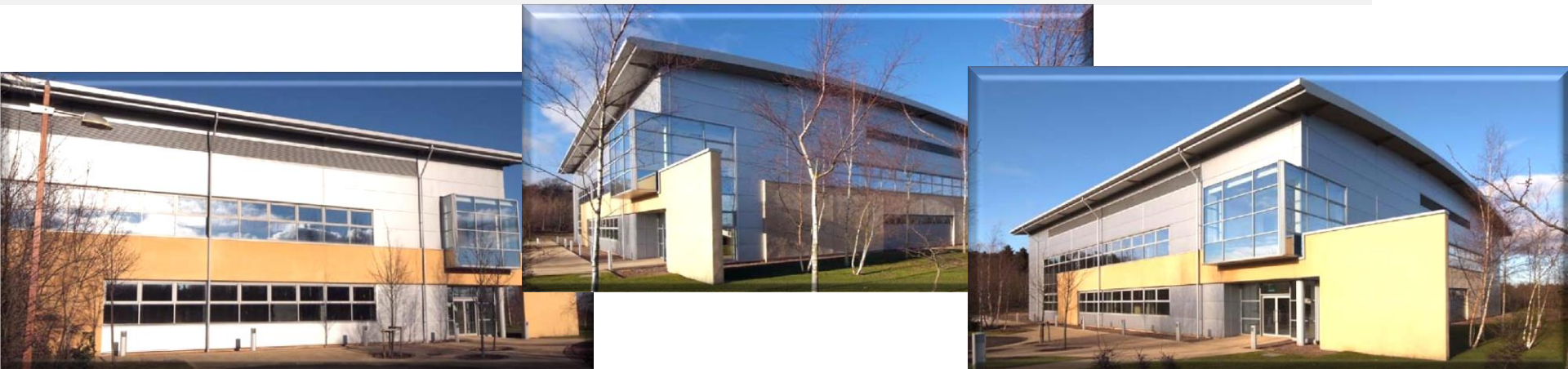


BVL Braintree facility capabilities

- › **Braintree Biotechnology Building** – under development completion due January 2016
 - Automated Egg processing/Monolayers- 5 Million eggs per annum.
 - Recombinant microbial fermentation - 100, 400, 1200lts Fermenter train.
 - Down stream processing – Alfa Laval disc stack centrifuge and chromatography.
 - New quality control laboratory.
- › **Warner Drive facility**
 - Roller Bottle monolayer
 - Cell Factories monolayer
 - Manual egg processing
 - Cell Bioreactors
 - Blending Fill and Freeze drying
 - Process development
 - Support function- Q.C., warehouse, cold store, packing....



BVL Biocampus facility (under development)



- BVL acquired freehold on the BioCampus 03/13
- Superb biotechnology development site
- Situated 8 miles from Edinburgh City Centre within a complex that includes, Moredun, Pentlands Science Park, Edinburgh Vet School & Edinburgh Technopole
- BioCampus building will provides 50,000 sq ft of under roof.
- Benchmark will develop a new state of the art vaccine facility specifically for high volume products and bulk antigens to help supply the growth of the company going forward.



BVL Biocampus – building concept



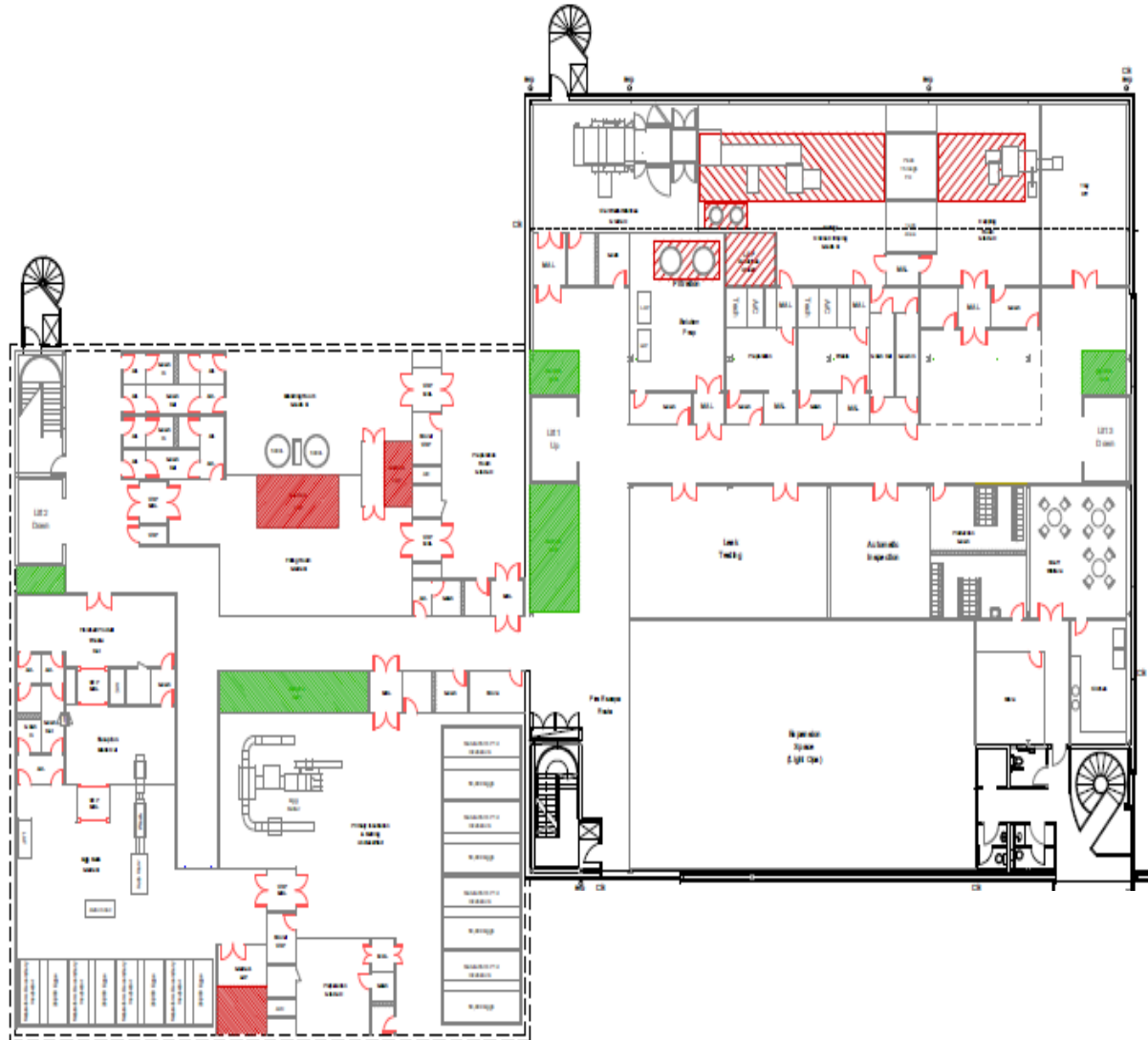


BVL – Building concept





Biocampus Manufacturing Floor approx 25,000 sq ft





Biocampus Facility planned capabilities

- › **Manufacturing**

 - High volume filling and freeze drying line – 120,000 single dose freeze dried vial batch size.

 - Flexible filling suite – 3000lt blend volume for 500ml or 1000ml packs, oily or aqueous types.

 - Flexible antigen production suite, automated egg or monolayers.

 - Support function- quality control, warehouse, cold store, packing...

- › **Animal health Division Head Quarter Functions**

 - Sales and marketing

 - Administration and HR

 - Finance

 - R&D

 - IT

 - Development laboratory



Benchmark
Animal Health



Benchmark
Vaccines Ltd

Technology



Virus Like Particle Development projects

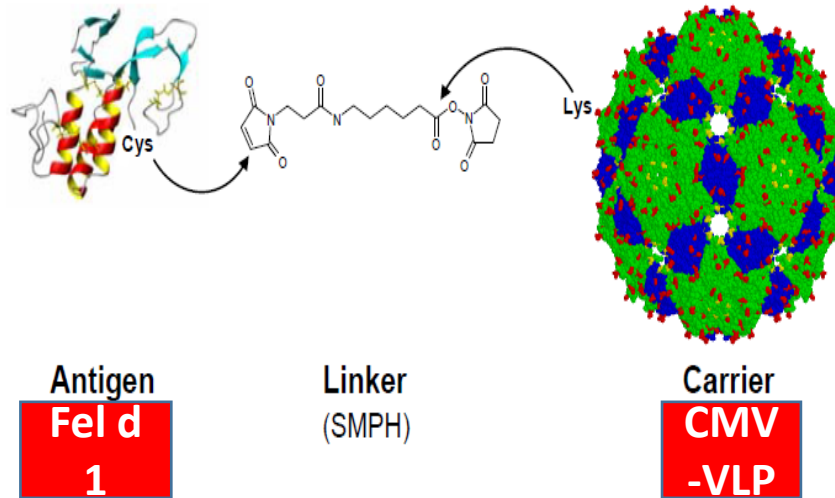
- **Hypocat-** Neutralises major cat produced human allergen (Fel d 1), 10% of people are allergic to cats. The development is a recombinant Cucumber Mosaic Virus linked to recombinant Fel d 1. It is a unique development with no competitor product in cats. Sales are forecast to be in the region of £250M pa.
- **Canine Atopic Dermatitis (CAD)** for treatment of dogs 10% of whom suffer from this condition. The Development is recombinant Cucumber Mosaic Virus linked to a number of recombinant interleukins. The CAD market is in excess of £1Billion pa and is the biggest veterinary problem in dogs mainly treated by immunosuppressive drugs which have to be taken for life. (e.g. Zoetis - Apoquel)
- **Sweetitch-** For prevention and treatment of an allergy to insect bite, 10% of Horses are affected by the disease. The allergy is caused by the insect Culicoides (midge) and causes severe pruritus (itching) then lesions. The estimate market size is around £100M, currently there is no effective



Virus Like Particles Vaccines-Hypocat

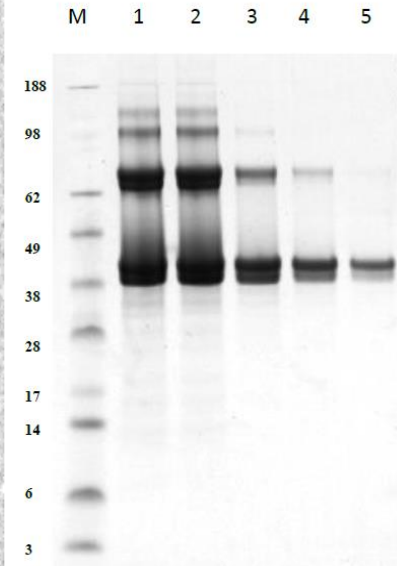
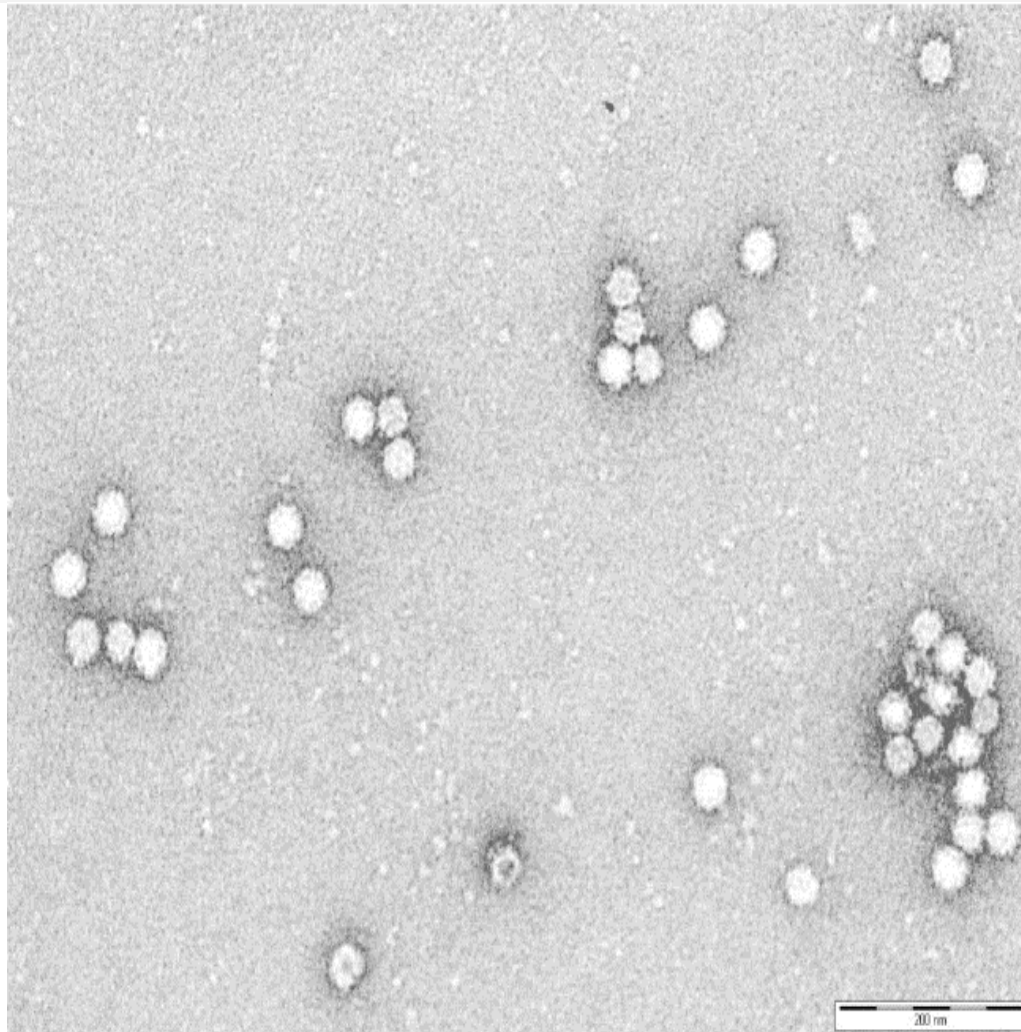
The Production Process

Antigen Coupling



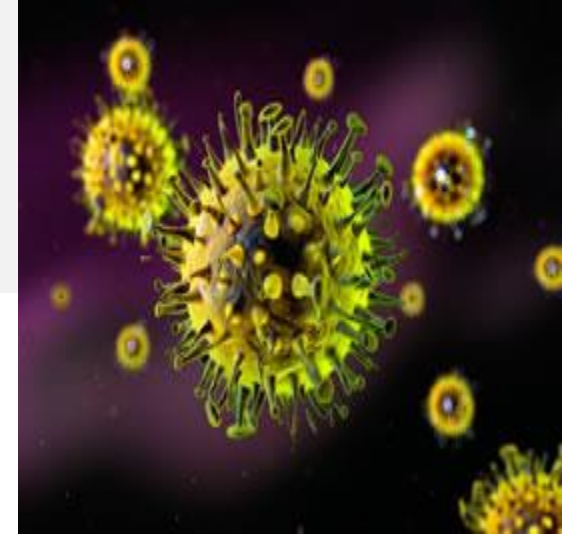


Electron micrograph of a BMK VLP vaccine





VLP vaccines



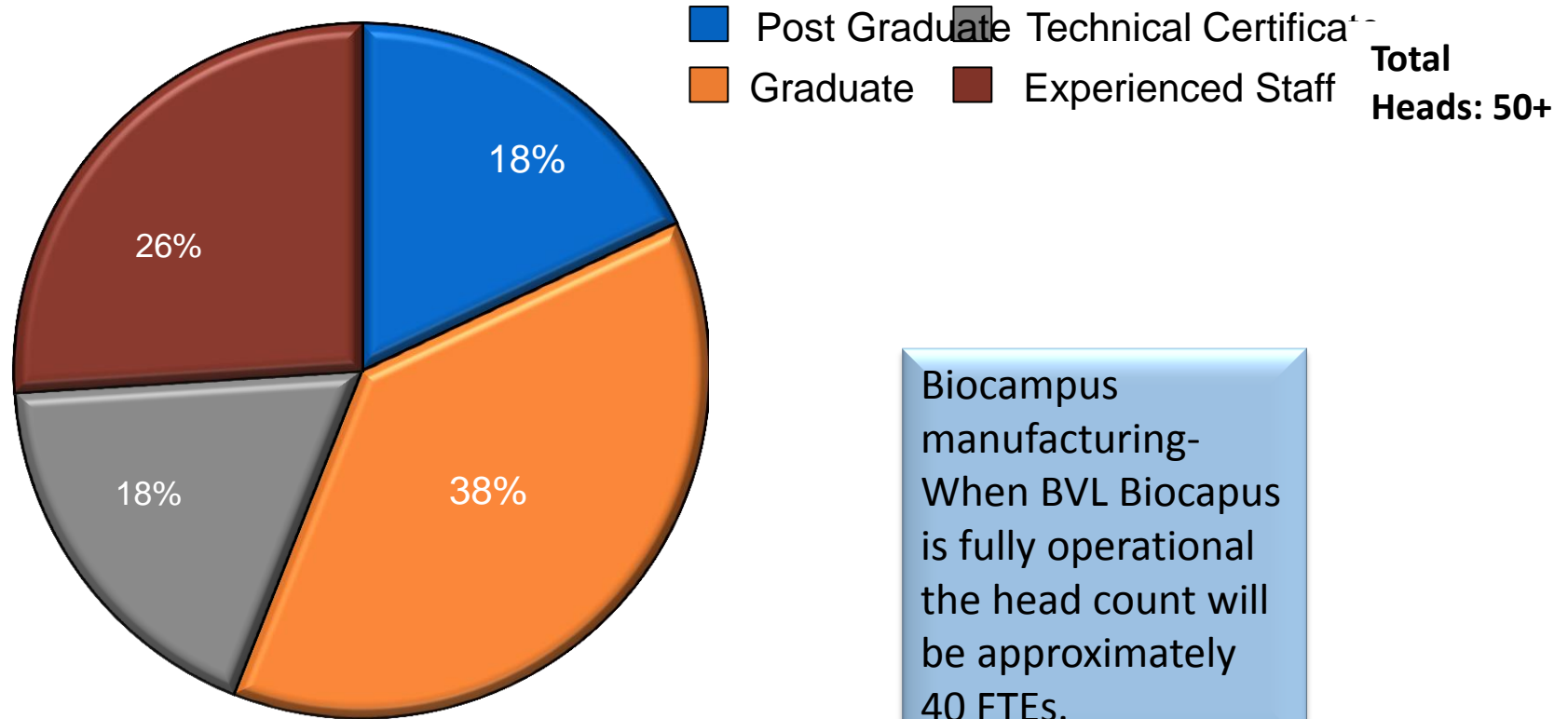
- Safe – non infectious
- Low cost of good – expressed in yeast and E.coli via bulk fermentation
- Powerful immune response – T cell and B cell.
- Adjuvant effect -contains host RNA which acts as a self adjuvant (via TLR 7)
- Low dose required
- Able to induce auto immunity to modulate immune system (CAD and Hypocat)
- Tried and tested in Human market
- Renewed interest for human flu and HIV
- Can be used carriers for other antigens or use own surface antigens



People



BVL Staff Qualifications



BVL Site Management Team



Bob Long

MSc, C.Biol, MRSB, QP
Managing Director

35+ years experience in manufacture and development of human and veterinary biologicals.



Simon Knight BSc (Hons)

Quality Manager

12 years experience in Human Pharmaceuticals and 9 years in Quality Assurance.



James Northfield

BSc (Hons)
Production Manager

25+ years experience in manufacturing human pharmaceuticals and veterinary biologicals, in QA and Production



Chris Shaw BSc (Hons)

Development Manager

10+ years of experience in veterinary biologicals and human pharmaceutical manufacture.



James Mumford BSc (Hons)

ACMA, CGMA.
Finance Manager

10 years experience in Brewing, electronics, logistics and building industries.



Neil Goodman BSc (Hons)

C.Biol, MRSB
Technical Supply Chain Manager

25+ years of experience in veterinary biologicals manufacture and supply chain.



Mo Mohammed
MSc, C.Biol, MRSB
Project and Facilities Manager

20 years experience in biological manufacture and process engineering management



BVL Quality EU GMP + BVL is developing ICH Q10

Braintree Quality Metric Dashboard







Quality Management System Status



100 % of systems in compliance

Quality Management System Status Colour Key





-  **Controlled** (Site in adequate control if 11-14 systems are in a state of "Control" or "Attention needed" and no system in a state of "Inadequate control" for 3 or more consecutive months)
-  **Attention needed - improving trend** (Site in "Attention needed" state if 3-4 systems are in a state of "Inadequate Control" or any system is in a state of "Inadequate control" for 3 or 4 consecutive months)
-  **Attention needed - worsening trend** (Site in "Attention needed" state if 3-4 systems are in a state of "Inadequate Control" or any system is in a state of "Inadequate control" for 3 or 4 consecutive months)
-  **Inadequate control. Action required** (Site in "Inadequate control" state if 5 or more systems are in a state of "Inadequate control" or any system is in an a state of "Inadequate control" for 5 or more consecutive months)

Summary

Timely completion of change control actions still continues to present a challenge to the site due the significant amount of change occurring. The limits for change control actions have been changed from Alert limit = 20 to Alert limit = 50 and from Action limit 20 to Action limit 50 to account for the expected increase in change actions due to the commencement of the BBB project. Although the site is in control, HA/customer audit actions and change control actions are still significant in number and being monitored (see Quality Management Review meeting minutes for resource discussions)

Breakdown of System Compliance

System	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15
Batch Release	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Calibration	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Change Control	Yellow	Red	Red	Yellow	Yellow	Red	Red	Red	Red	Green	Green	Green	Green
Complaints	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Deviations	Yellow	Yellow	Red	Red	Red	Red	Yellow	Red	Red	Green	Green	Green	Green
Documentation Management	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Laboratory control / OOS	Green	Yellow	Green	Green	Green	Green	Red	Green	Green	Green	Green	Green	Green
Preventive Maintenance	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Product, Process and Facility Control	Red	Red	Red	Yellow	Green	Green	Green	Green	Green	Green	Green	Green	Green
Stability	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Supplier Management	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Surveillance	Yellow	Yellow	Green	Green	Green	Green	Green	Green	Yellow	Yellow	Yellow	Green	Green
Training	Green	Green	Green	Green	Green	Red	Green	Green	Red	Red	Green	Green	Green
Validation and Qualification	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green

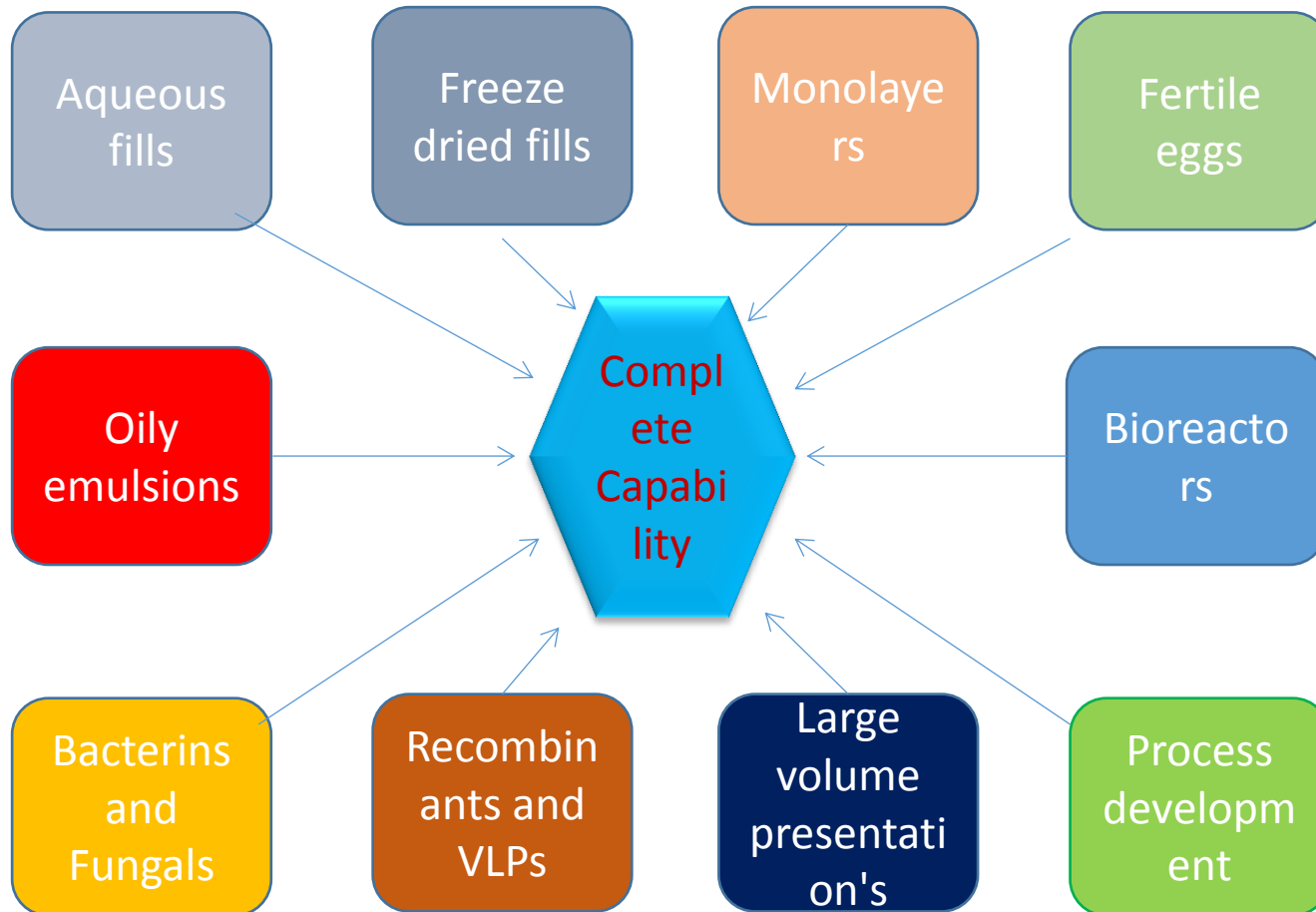
-  System is within the Alert limits
-  System is outside Alert limit but within Action limits and is a worsening or static trend from the previous month
-  System is outside Alert limit but within Action limits and is an improving trend from the previous month
-  System is outside the Action limits



End Slide



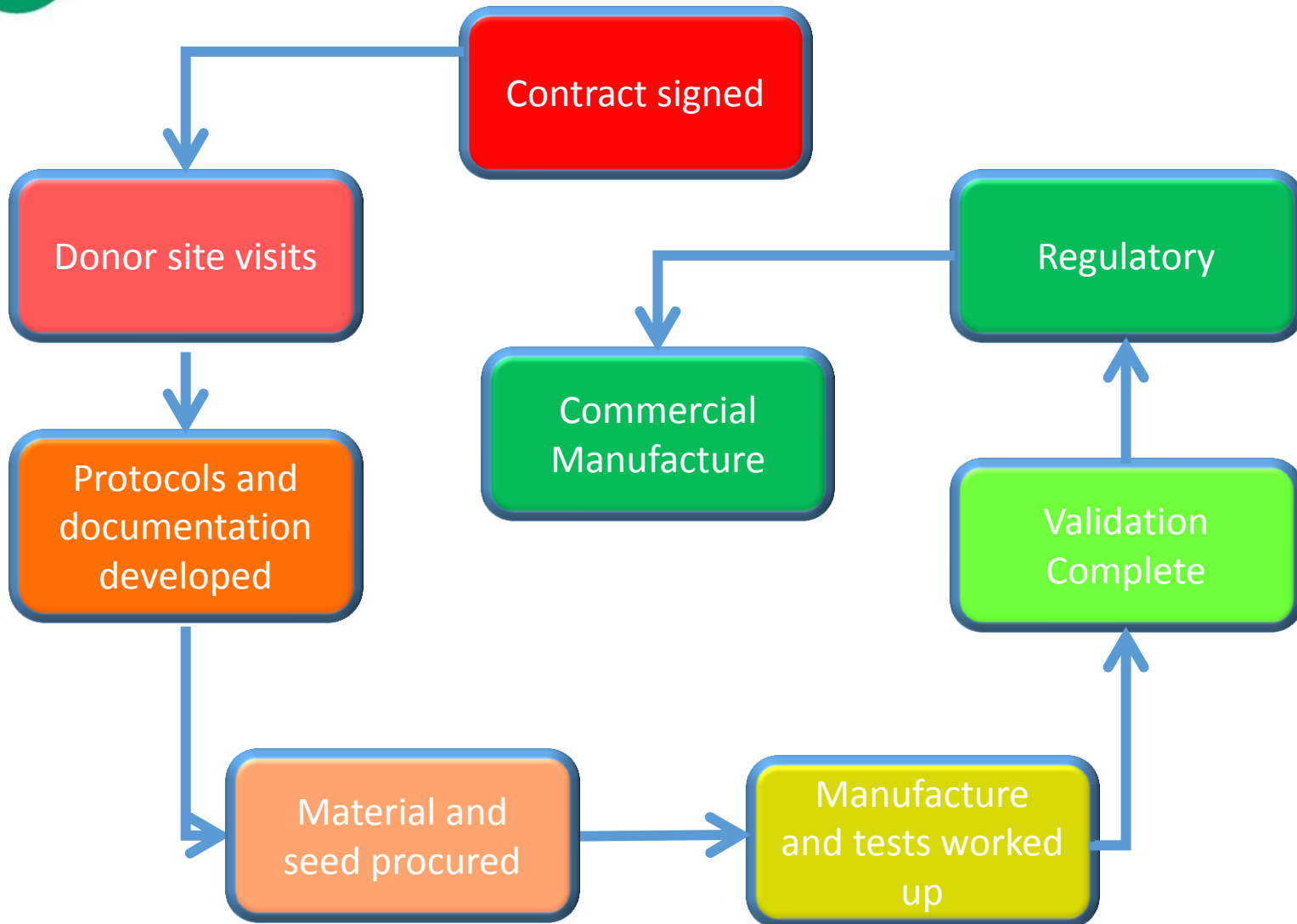
Conclusion





Benchmark
Vaccines Ltd

Technology Transfer



Vaccine development at Moredun



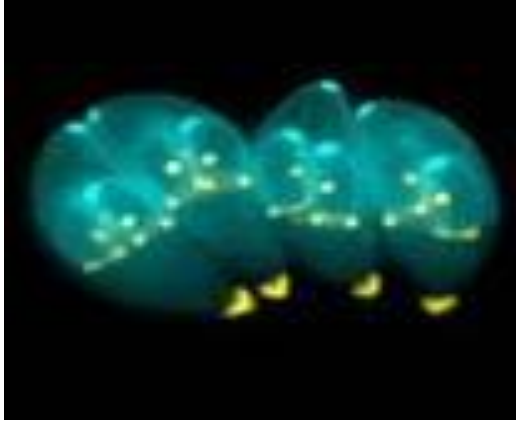
Dr. Alasdair Nisbet

Head of Vaccines Pillar

Moredun Research Institute

Moredun Research Institute

Vaccines Pillar



Viruses, Bacteria and Parasites

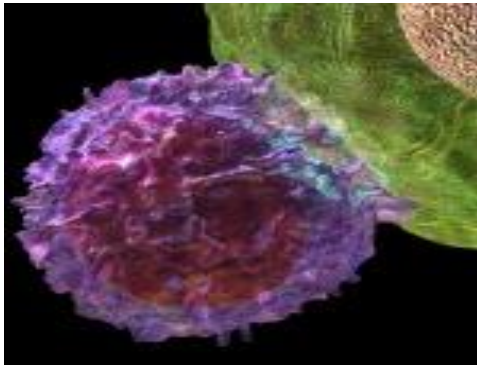
Host-pathogen interaction

Immune responses

protective

immuno-pathology

pathogen evasion

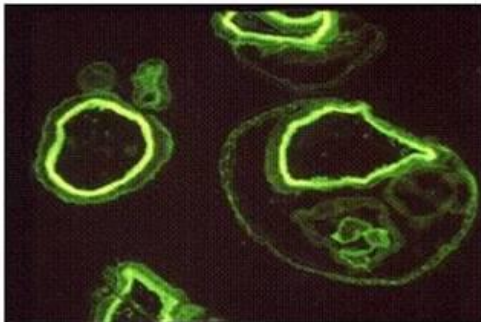


Vaccination

live

killed

recombinant

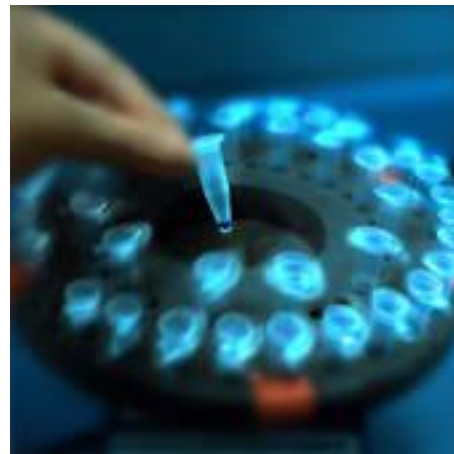


Outputs

- Vaccines
- Diagnostics
- Disease control strategies
- Epidemiology and Surveillance



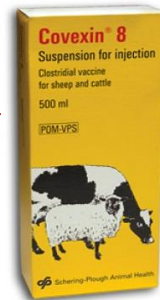
Knowledge exchange
Spin Out Companies
Contract research
Education and training



Some Moredun Vaccine Successes

Braxy
(*Clostridium*
septicum)

Lamb
dysentery
(*Clostridium*
perfringens
type B)



Louping ill
virus



Pasteurella
pneumonia

(*Mannheimia*
haemolytica)



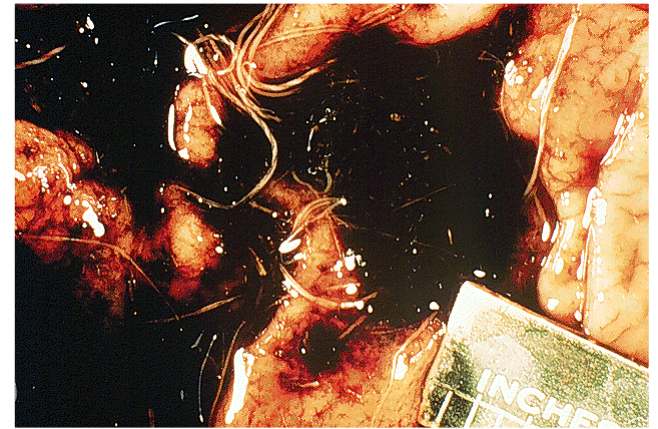
Ruminant nematode vaccines

- research > 50 years
- practical outcomes
 - *cf.* other pathogens: disappointing
- few successes
 - irradiated vaccine
 - bovine lungworm



Haemonchus contortus - most important gastrointestinal nematode of sheep in tropical/subtropical regions

- Acute disease can be fatal
- High FEC (2000 to 20000 EPG) - difficult to control
- Anthelmintic resistance widespread



Haemonchus vaccine development at Moredun

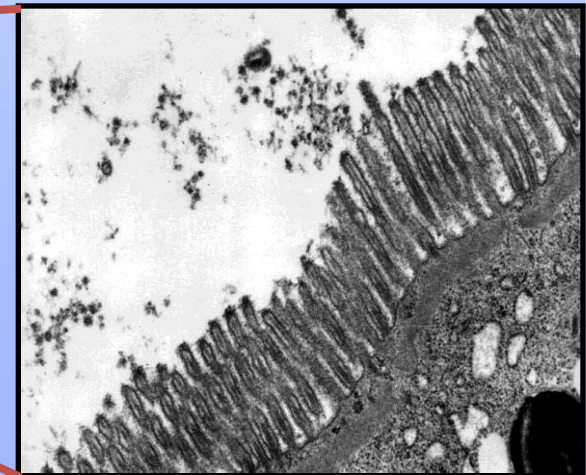
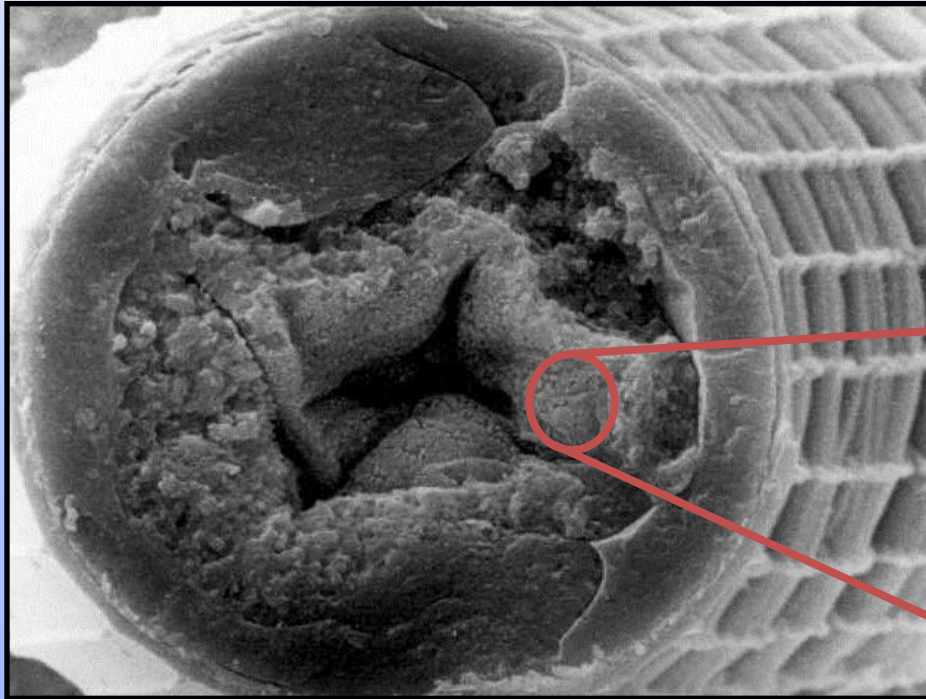


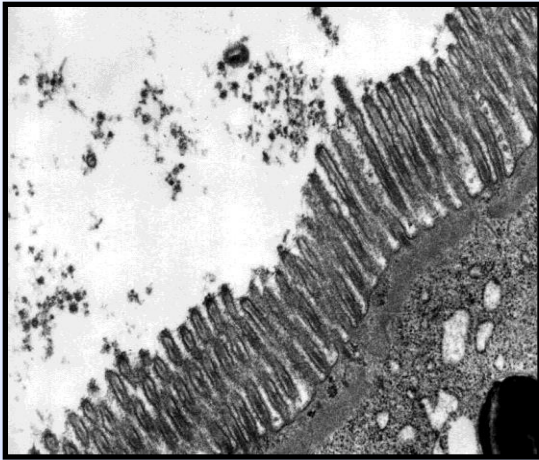
and Department of Food and Agriculture, WA



Haemonchus vaccine - gut antigen approach

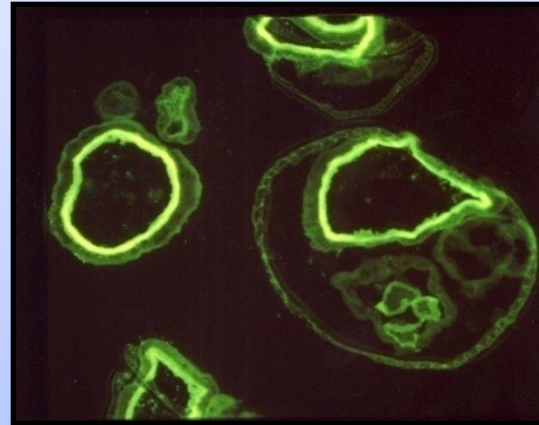
Because *Haemonchus* feeds on blood, molecules on the surface of the worm's gut are appropriate vaccine targets





When surface proteins from the worm gut are injected into a sheep.....

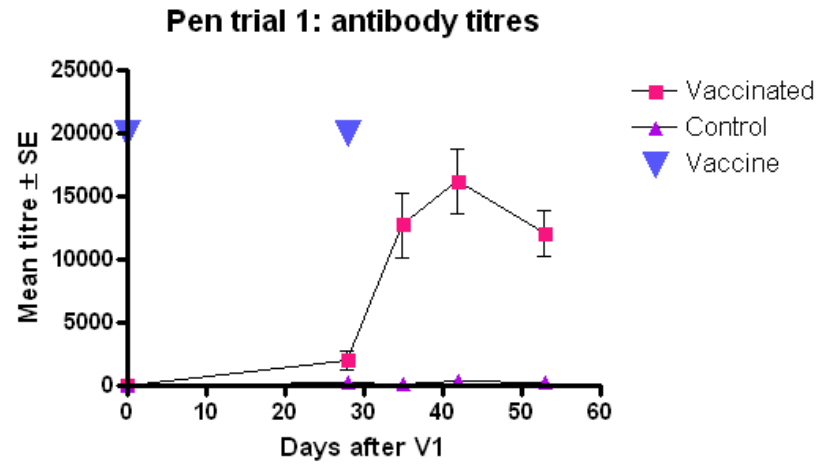
it responds and makes antibodies which circulate in the blood. If a vaccinated sheep gets infected, the parasites ingest blood so that antibodies bind to the worms intestines ...



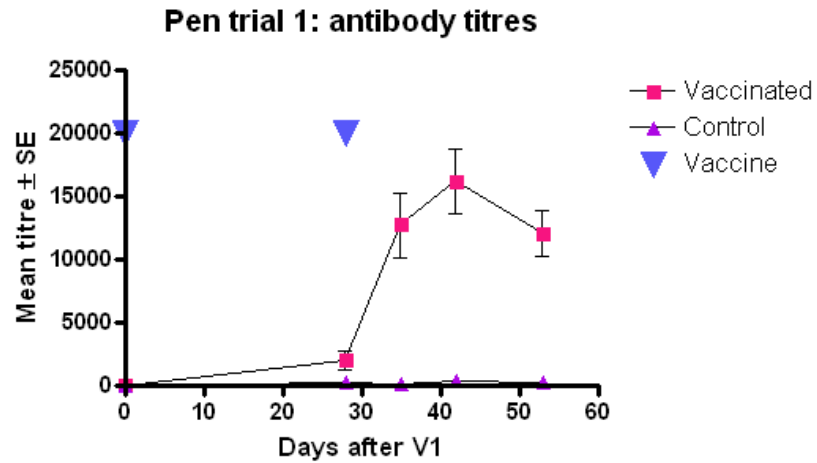
....leading to greatly reduced egg output and worm numbers.



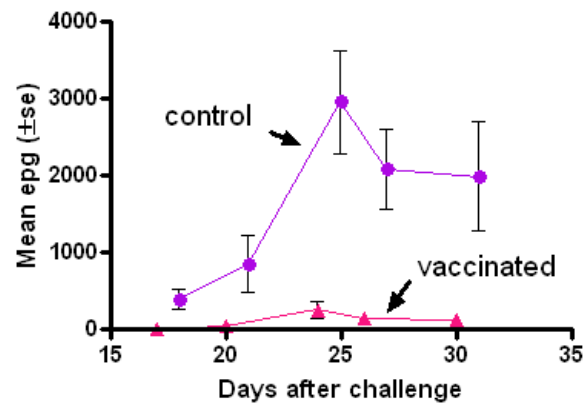
Pen trial example



Pen trial example



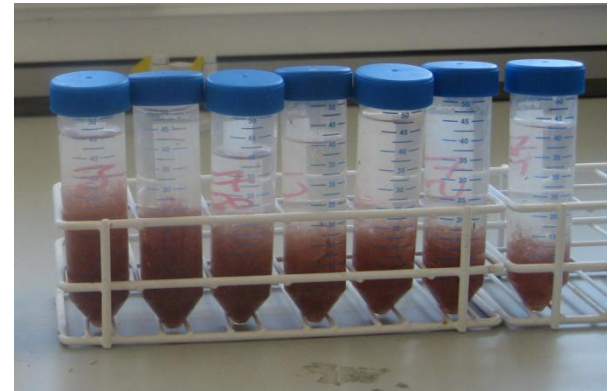
Pen Trial 1: Faecal egg counts of vaccinated and control sheep



Machine for rapid recovery of adult Haemonchus from infected abomasum

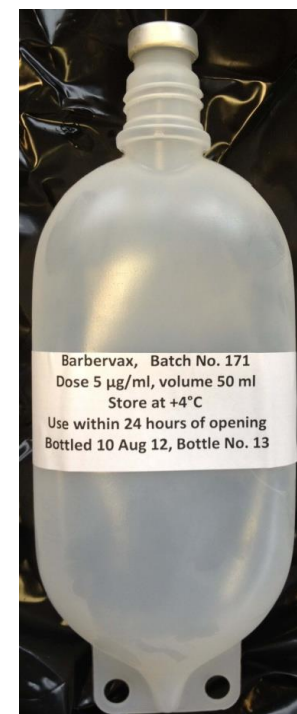


2 mins

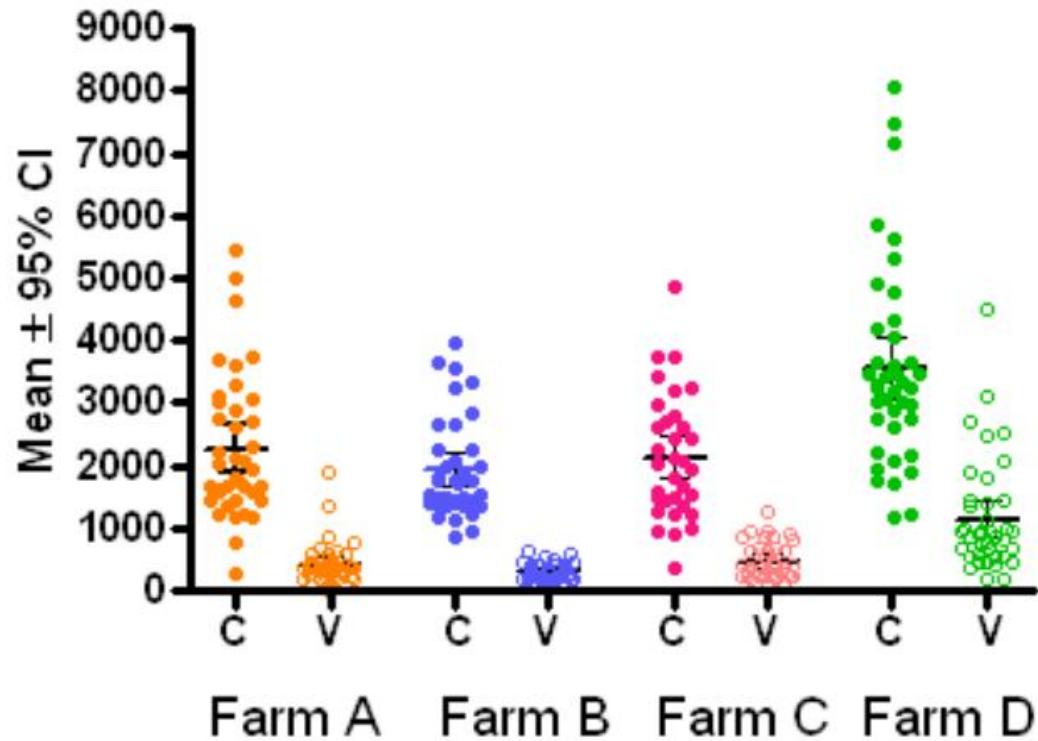


Good Manufacturing Licence granted by APVMA in 2010

Whole process from sourcing sheep to bottling vaccine



Effect of vaccine on Haemonchus egg output on four NSW farms from early Nov 2011 to late April 2012



>80% protection on each property



APVMA
Registered
October 1st,
2014



All 300,000
doses of vaccine
sold by word of
mouth within
10 days

No large
pharma
involved

Conclusions and future directions

- Historically, Vaccine development from identifying cause of disease right through to manufacture
- Commercial success of vaccines against viruses, bacteria and nematodes
- Current projects to develop vaccines against major endemic, production limiting diseases in sheep, cattle, poultry and farmed fish



MoreDun

www.moredun.org.uk

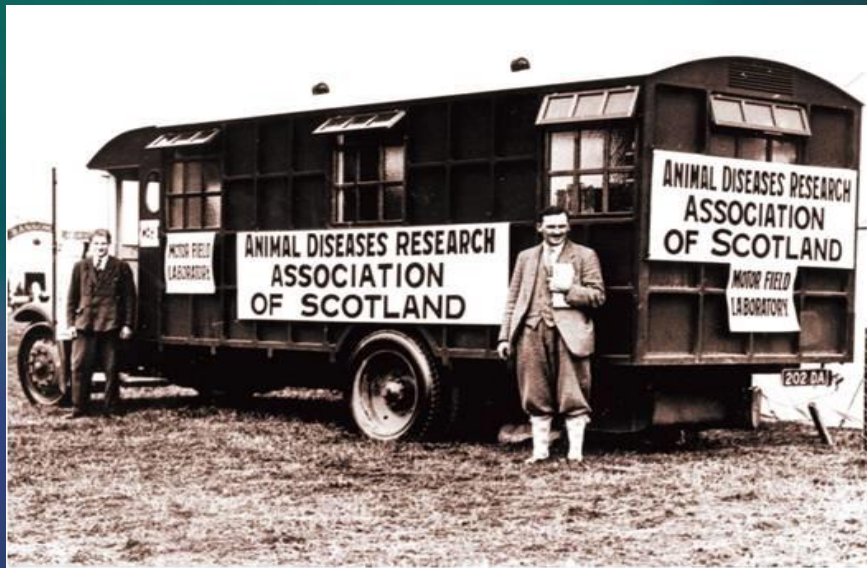
Visit by Taiwanese delegation

September 2016



Moredun Research Institute

*“To lead in livestock health solutions
for global food security”*



The Moredun Group

Moredun Foundation

Moredun Research
Institute

Pentlands
Science Park

Moredun
Scientific Ltd



History and ethos



Membership, history and ethos

Set up by farmers in 1920 and still governed by farmers

Focus on useful outputs that impact farming communities

Vaccines

Diagnostics

Disease control Programs

Public-Private Partnership - charity

Academic endeavour

National and regional economy

Financial returns to support further research



Moredun Research Institute

Infectious endemic livestock diseases of relevance to Scotland, UK, EU and worldwide



Livestock sector in UK contributes £ 8 Billion

Losses associated with disease £ 1 Billion

Food security: Demand for food expected to increase by 40% in 2030 and by 70% in 2050

Dietary shifts: Emerging economies

Increase sustainable efficiency of livestock production, improve welfare and reduce waste

Group Resources



- Over 200 staff from many disciplines
Bacteriology, Virology, Parasitology, Epidemiology



- Category II and III containment for animal and lab work
 - Ability to work in large and small animal systems
 - real disease state
 - Surgical and Gnotobiotic facilities
 - Can run to quality standards GMP / GLP / vGCP



- Strong international connections
- Strong national and local connections
 - Farming community
 - Academic and commercial collaborations

Achievements at Moredun

- Identification of the cause of 18 diseases
- Characterisation of the pathogenesis of 23 diseases
- Development of vaccines for 11 diseases
- Development of treatment strategies for 12 diseases
- Surveillance service for 36 diseases



Collaborations

- Knowledgescotland partnership
- EBRC
- Roslin Institute
- University of Edinburgh
- University of Glasgow
- Heriot Watt University
- University of Stirling
- SPASE
- EPIC
- CoZEE

AgResearch /Hopkirk NZ

Vaccine and Infectious Disease Organisation Canada

USDA

National Veterinary Institute Sweden



Moredun Scientific

A contract research organisation providing research and testing services to the **Animal Health** Industry and **BioPharmaceutical** Industries



Animal Health Industry

Client base:

Pharmaceutical companies developing & marketing new veterinary medicines (e.g. vaccines and therapeutic drugs) for livestock.

Example clients : Zoetis, Elanco, MSD-Animal Health

Portfolio of services:

Efficacy studies – clinical trials in livestock experimentally infected with a specific pathogen (bacteria/virus/parasite)

Safety studies - trials to test that the potential new veterinary medicinal product is safe in the target animal.



Biopharmaceutical Industry

Client base:

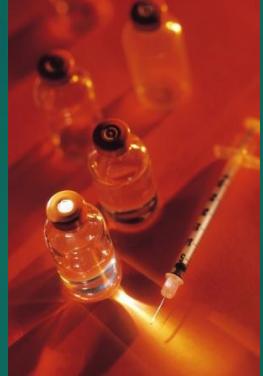
Companies developing & manufacturing human or veterinary biopharmaceuticals.

Portfolio of services:

Biosafety testing services to ensure that the biopharmaceuticals (and cell lines and raw materials used in their manufacture) are free from biological contaminants such as bacteria, viruses, fungi.

Regulatory compliant tests.

Tests conducted to Good Manufacturing Practice (GMP) or Good Laboratory Practice (GLP) as appropriate.





Moredun

www.moredun.org.uk



Benchmark
Animal Health

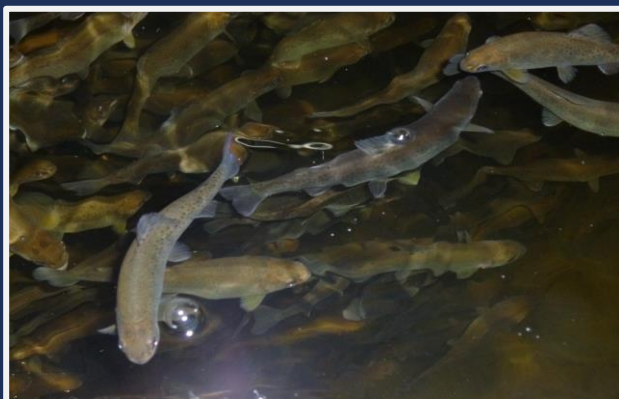


Moredun

Kim D. Thompson

Aquaculture Research Group

Moredun Research Institute





Benchmark
Animal Health



Partnership

- 18 years of diagnostic expertise in fish diseases.
- Knowledge of global fish vaccine markets.
- Established customers.
- Collaboration within fish health research industry

<http://bmkanimalhealth.com/>

A
R
G

- Est. 1923. Expertise in vaccine development.
- Knowledge in broad range of bacterial species.
- Infrastructure in place
- Proteomic suite, molecular laboratories available

<http://www.moredun.org.uk/>



The Aquaculture Research Group
established April 2013

INTRODUCTION TO BENCHMARK

Founded in 2000 to build a company that progresses...

- Good health and welfare of animals
- Sustainable business
- Knowledge transfer
- Robust animal breeding and genetics

by building...

- A world-class team
- Next-generation scientific research & production capacity

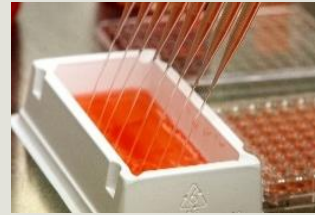
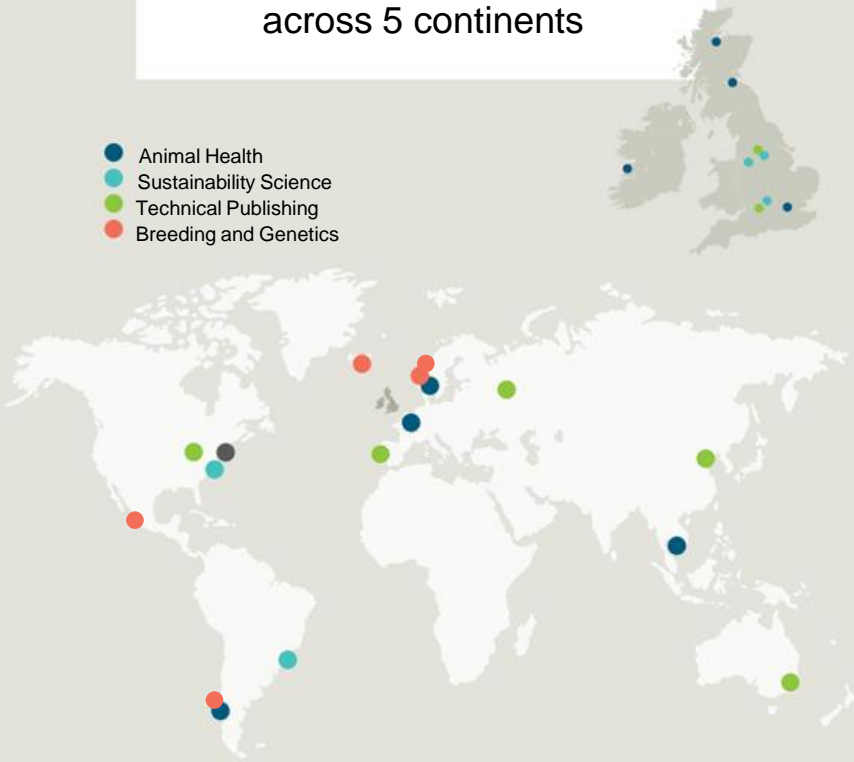


BENCHMARK AT A GLANCE

First class team with expert knowledge and practical experience

396 people in 15 countries across 5 continents

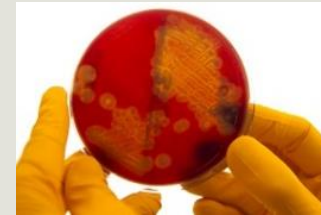
- Animal Health
- Sustainability Science
- Technical Publishing
- Breeding and Genetics



Provider of products and services to the agriculture and aquaculture industries



State-of-the-art aquatic health clinical and diagnostic laboratories in North America, Europe and Asia



£6.5m investment in research and development



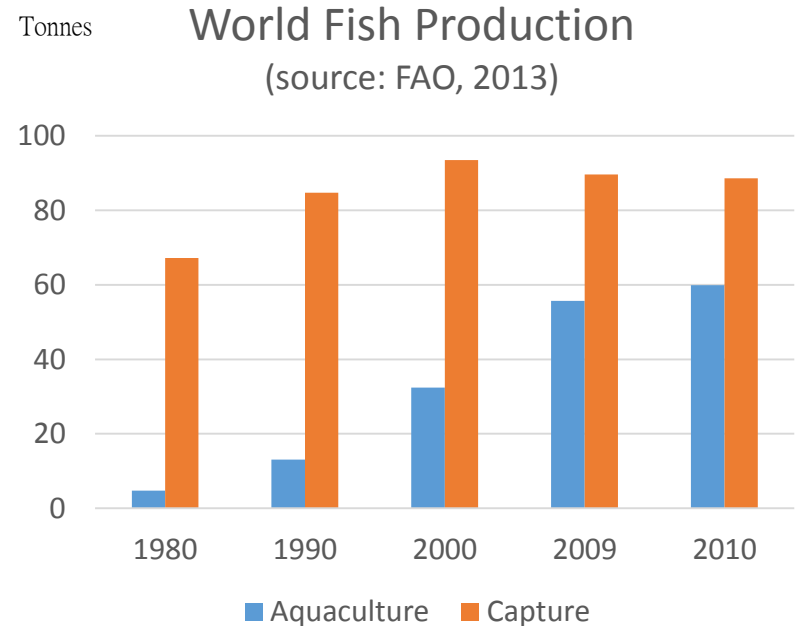
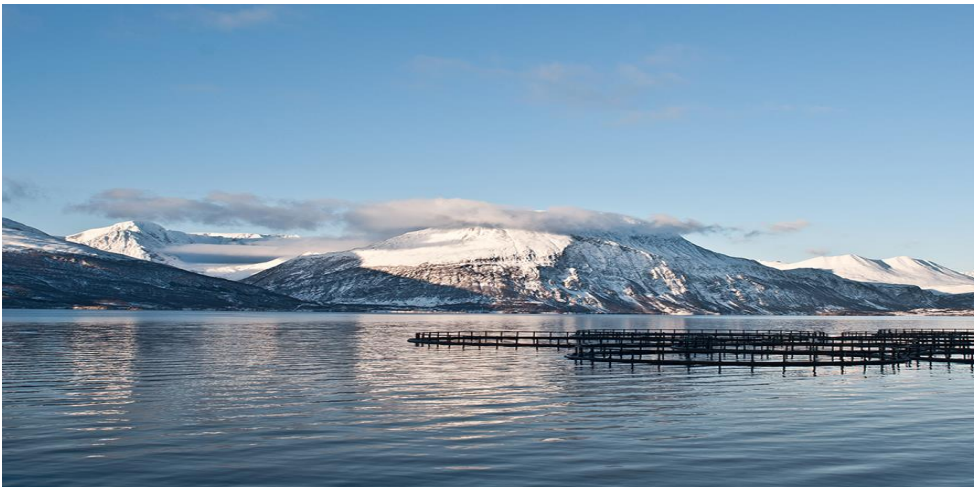
Sustainable research farms in England, Scotland and Brazil



Long-term partnerships with scientific centres of excellence

Global Aquaculture

- Aquaculture is most rapidly growing animal food production sector
- Cultured fish production increased from 34.6 to 59.9 m tonnes from 2001 to 2010
- Total capture production remained around 90 million tonnes since 2001



- Aquaculture produce is a valuable traded food commodities
- In 2010, the value of aquaculture production was estimated at £74.3 billion
- Over 220 species of finfish and shellfish cultured globally

Scottish Aquaculture



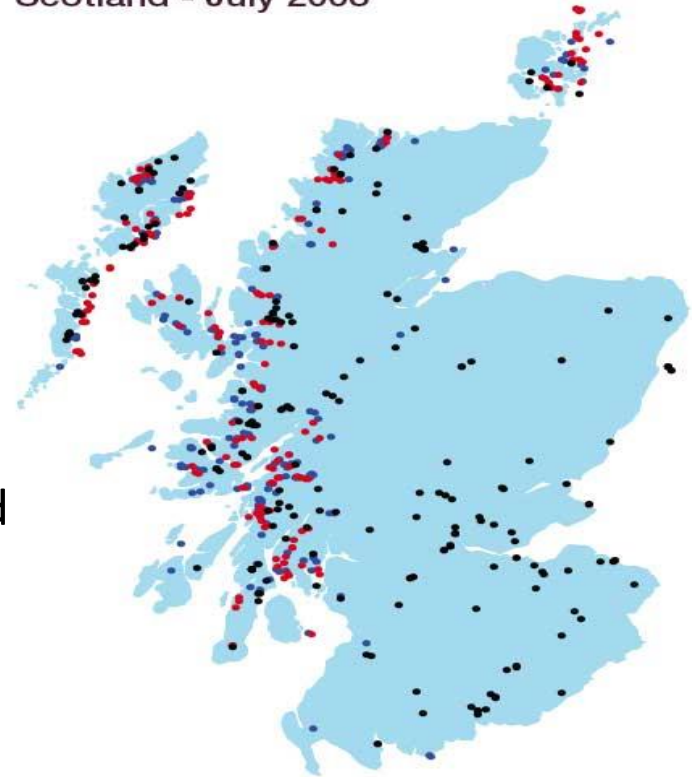
Atlantic salmon




- Main cultured species
- The largest salmon producer in the EU and the third largest globally
- Production 162,223 tonnes worth £ 537 million (2012)

Other Species

- Rainbow trout - 5,670 tonnes
- Brown trout - 42 tonnes
- Halibut - 73 tonnes
- Arctic charr - 0.2 tonnes

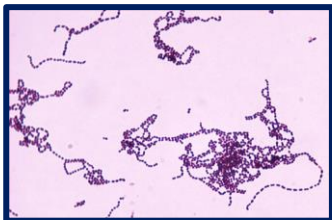
Active Fish and Shellfish Farms in Scotland - July 2008



	Sea water farms
	Fresh water farms
	Shellfish farms

Aquaculture and Disease

- Pathogens and parasites are estimated to be responsible for 5-7% annual losses in finfish aquaculture
- Representing £3.7-5.2 billion in losses



<http://www.salmonfarmsireland.com>

Health Management

- Good husbandry practises
- Rapid detection of pathogens
- Prevention of disease by vaccination and other immunotherapies
- Use of chemotherapeutants



Commercially Important Pathogens

Bacteria

- *R. salmoninarum*
- *M. viscosa*
- *P. salmonis*
- *V. ordalli*
- *V. angillarum*
- *V. salmonicida*
- *E. ictaluri*
- *P. damsela*
- *S. iniae*
- *S. agalactiae*
- *A. salmonicida*
- *A. hydrophila*
- *F. psychrophilum*
- *L. garviae*
- *T. marinarum*
- *Y. ruckeri*



RNA Virus

- IPNV
- SPDV
- IHNV
- VHS
- VNN
- ISAV
- SVC
- SDV

DNA Virus

- EHN
- KHV
- IRV



Parasites

- (endoparasites)
 - Myxosporean
- (ectoparasites)
 - Monogean
 - Caligean



Amoebic gill disease (AGD)

- Gill disorder of marine fish,
- Greatest impacts in cultured Atlantic salmon. Disease endemic in Tasmania, Australia, costing A\$230m (£128m) a year.
- AGD is now a major disease to Scottish Atlantic salmon aquaculture industry



Atlantic salmon gills infected with Amoebic Gill Disease caused by *Paramoeba perurans*

²<http://www.vetinst.no/Faktabank/Amoebegjel/lesykdom-AGS-amoebic-gill-disease-AG>



<http://www.salmonfarmireland.com/search?updated-max=2013-11-17T06:25:00-08:00&max-results=10>



Sea louse *Lepeophtheirus salmonis*

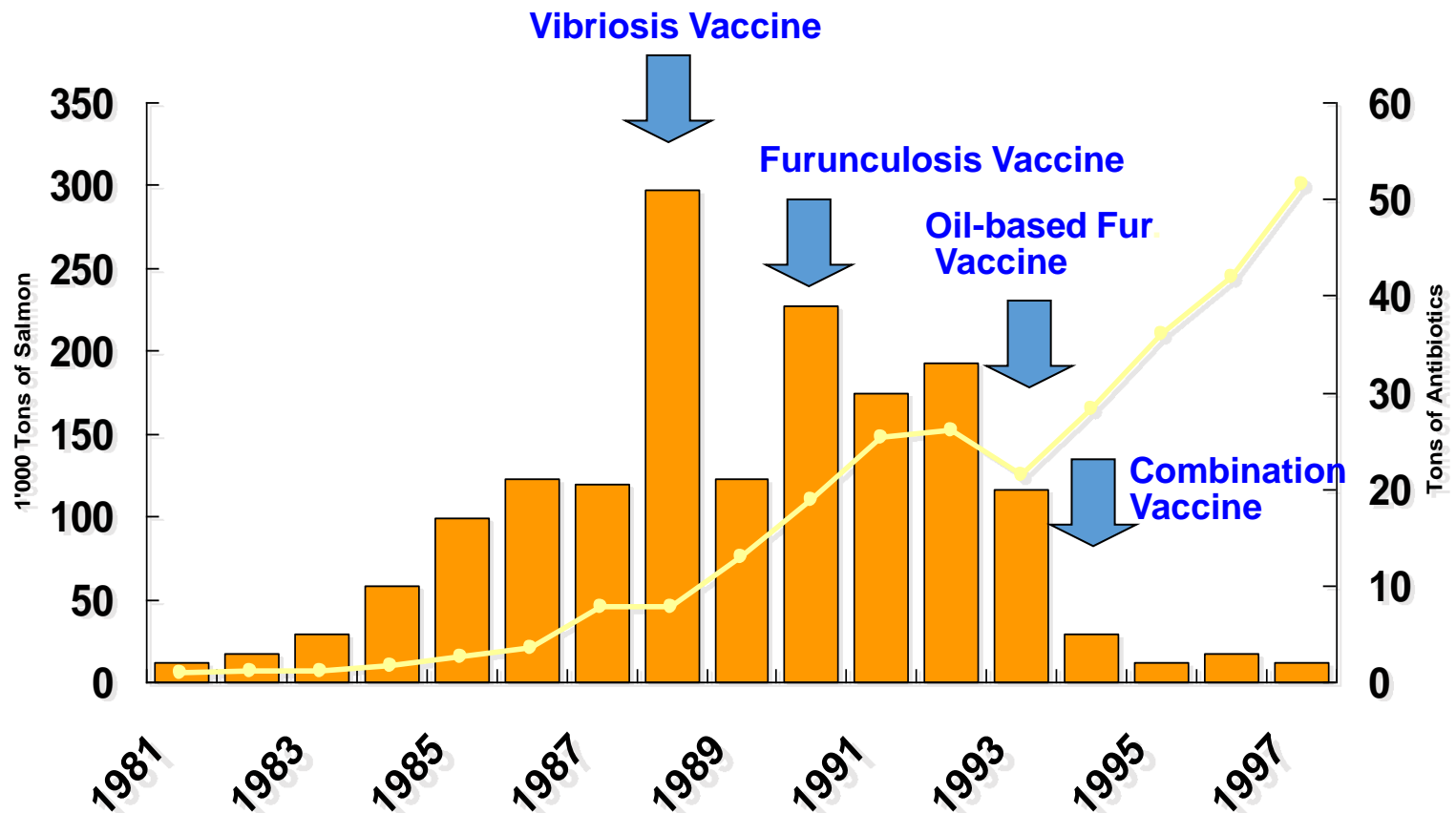
- Sea lice, parasitic copepods infecting salmon in the sea
- Costs the industry >£30M p.a. to control. Using various chemical treatments
- Alternative eco-friendly control methods being developed
 - Cleaner fish (wrasse and lumpsucker)
 - Vaccines

Vaccines for aquaculture

- Each year \approx 418 million salmon and \approx 90 million rainbow trout vaccinated globally
- Reduce the need for antibiotics and chemicals
 - Reduce problems with antibiotic resistance
 - Reduce environmental impacts
- Control significant diseases
- Increase productivity
- Save costs for farmer
- Improved animal welfare
- Major area for growth in aquaculture



Norwegian Salmon Production Consumption of Pure Antibiotics and Effect of Vaccines



Potential types of vaccines for aquaculture

- Formalin inactivated pathogen
- Live attenuated pathogen
- Tissue culture
- Purified macromolecules
- Recombinant
- Recombinant vector vaccines
- Synthetic vaccines
- DNA vaccines
- VLPs

their efficacies
range from
good to
marginal



Methods of Vaccine Delivery

Injection

- Most effective but need to anaesthetise and handle the fish
- Labour intensive
- Stressful for the fish

Immersion

- Practical for mass vaccination of small fish only
- Does not work for all vaccines

Oral

- Most suitable for mass vaccination but dosage uncertain and sometimes poor potency
- Less stressful to the fish
- Most often used as a booster vaccine

Injection Vaccination



Small 2 g rainbow trout

large scale in sea bass in Europe

Immersion Vaccination



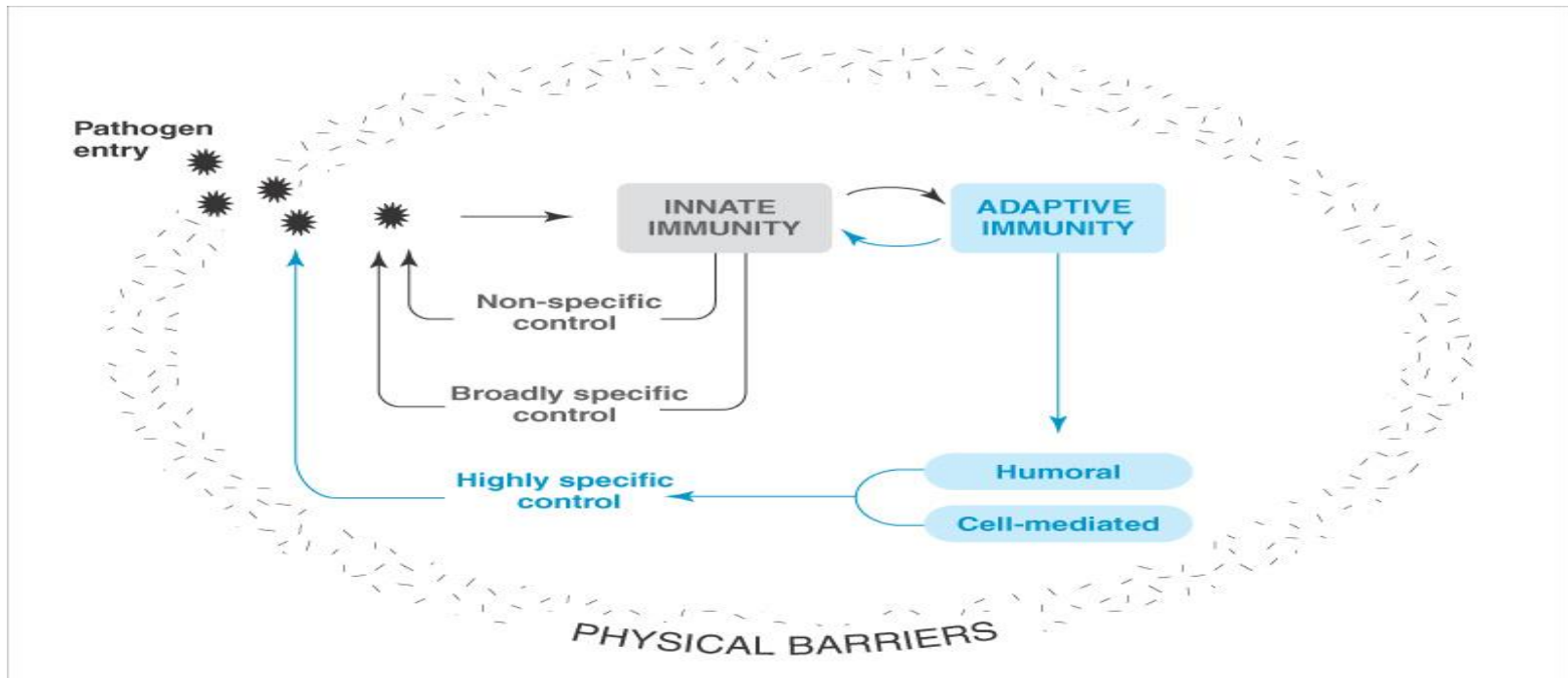
Oral Administration

Types of adjuvants

- Mineral oils
- Inorganic compounds e.g. alum
- Bacterial products
- Non-bacterial organics e.g. squalene
- Plant saponins
- Cytokines
- Pattern recognizing receptor (PRR) e.g. toll-like receptors (CpG oligonucleotides or poly I:C)
- Genetic adjuvants e.g. DNA plasmid vector expressing viral antigens (haemorrhagic septicaemia virus glycoprotein - DNA vaccine)
- Delivery systems

Fish's defence system against pathogens

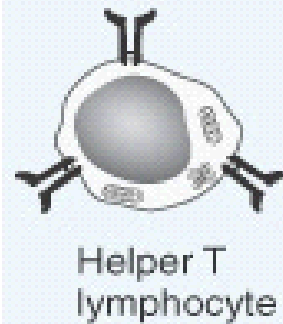
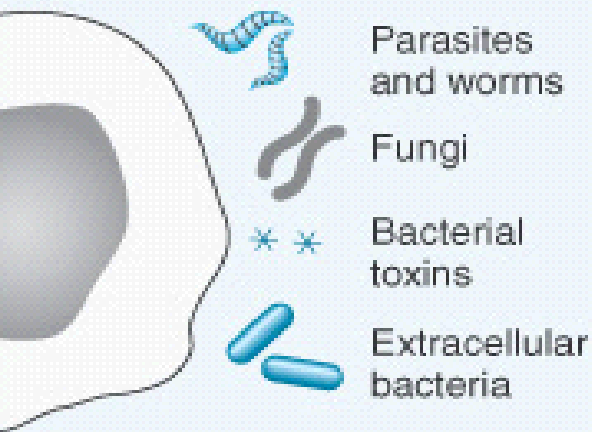
- Physical barriers
- Innate immune system (non-specific)
- Adaptive immune system (specific)



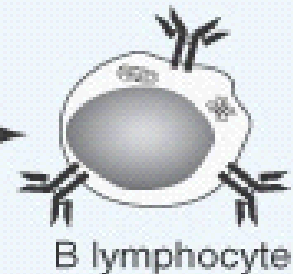
TYPE OF ANTIGEN

RESPONDING LYMPHOCYTES

Extracellular

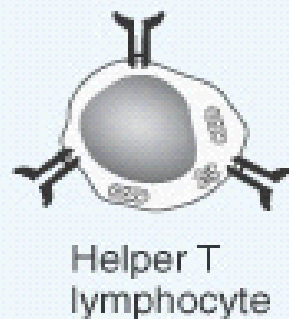
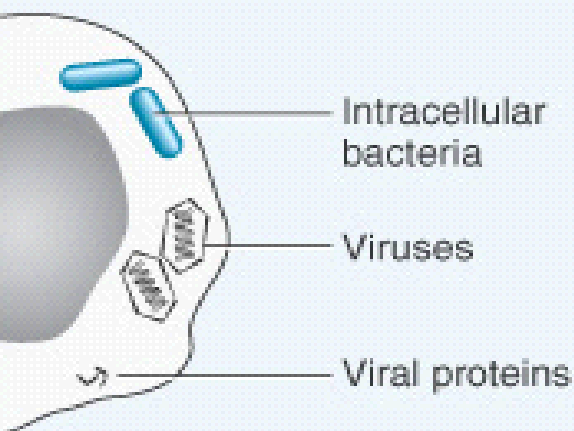


Soluble factors

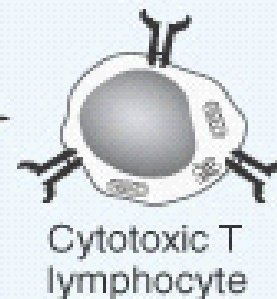


Matures to make antibodies against extracellular pathogens or their products

Intracellular

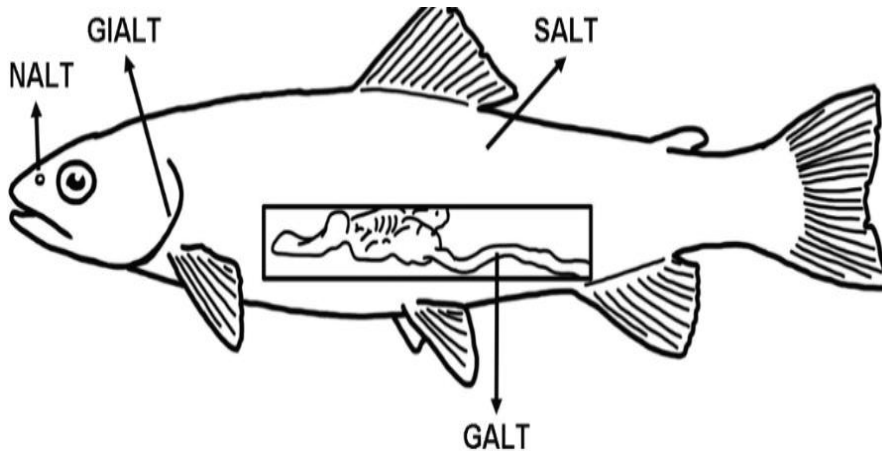


Soluble factors



Matures to lyse cells infected with intracellular pathogens

Mucosal Tissues



Schematic representation of the four teleost main mucosa-associated lymphoid tissues (MALT) described so far and their anatomical localization. GALT: gut-associated lymphoid tissue; SALT: skin-associated lymphoid tissue; GIALT: gill-associated lymphoid tissue; NALT: nasopharynx-associated lymphoid tissue.

Mucus very important defence mechanism in fish - helps to prevent infections

- complement
- lysozyme,
- IgT/IgZ
- alpha precipitins,
- natural agglutinins,
- lysins,
- lectins
- C-reactive protein (CRP)



Benchmark
Animal Health

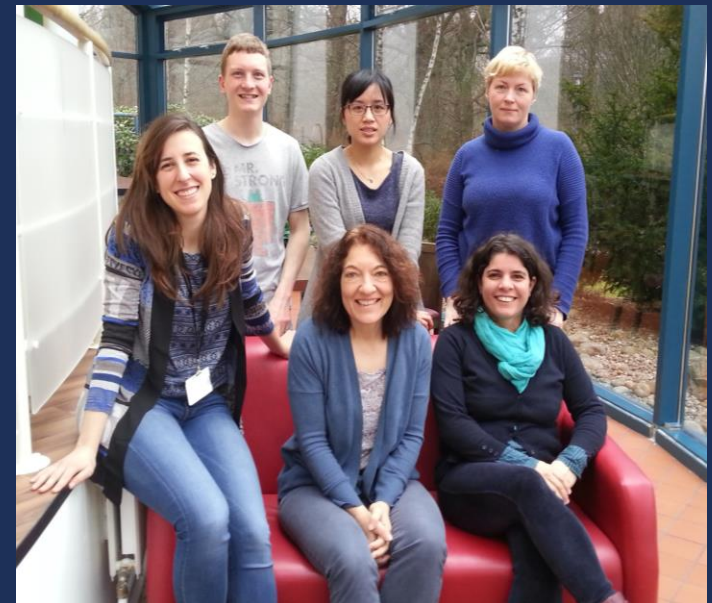


Moredun

kim.thompson@moredun.ac.uk

Our Progress since 2013

- ❖ Upgrade and Adapt Research Laboratories
- ❖ Expansion of Internal Scientific Expertise
- ❖ Establishment of a BioBank
- ❖ Initiate Research Activities
- ❖ Expand our Collaborations (National & International)



**“Barbervax”, the first vaccine in
the world for a worm parasite of
sheep**

**Invented, owned, commercialised
and manufactured by Moredun**

Barbers Pole worm

Globally, the most important roundworm parasite of sheep and goats

Blood sucker



Prefers warm climates

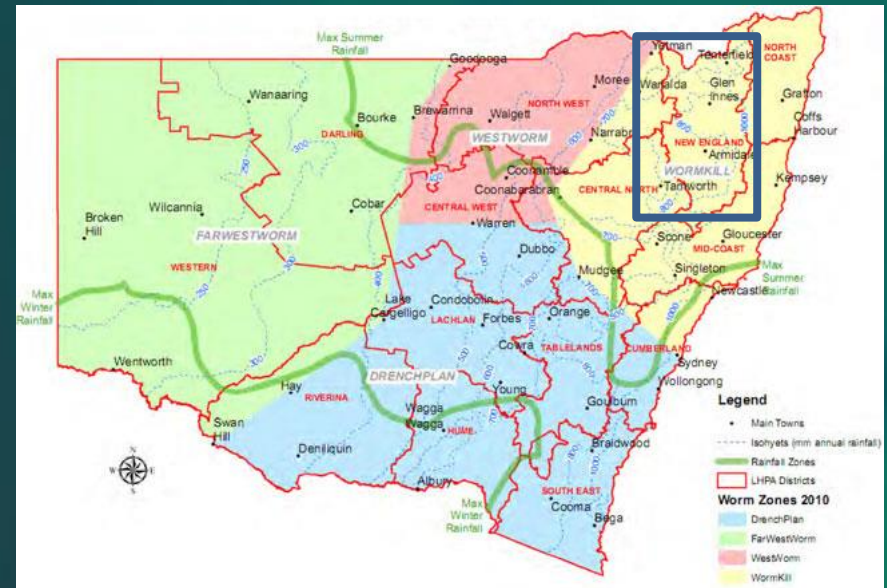
Resistance to drugs a serious problem

No vaccine available for this or any other species of gut worm of any host – until Barbervax was launched 18 months ago!



The biggest market is Australia

New England, North Eastern New South Wales.



New England – fine wool Merinos.

Flock size 3,000 to 50,000 in mobs of about 500

Barber's Pole Worm - their single most important cause of disease

Farmers treat 5 or 6 times a year, but drug resistant worms common



Armidale, New South Wales, Australia



Registered
October 1st,
2014, lambs
only

2m doses
sold in
first two
seasons.



Now
registered
for adult
sheep

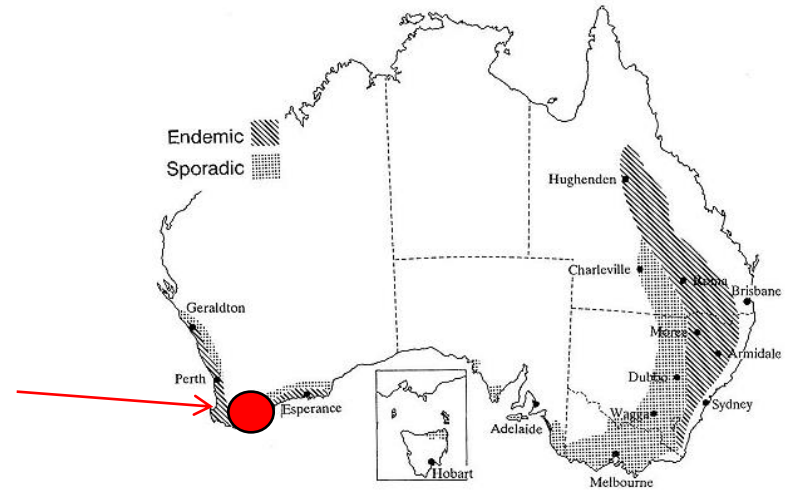
No large
pharma
involved

Manufacture of Barbervax in Australia?

Where?

(must be from Australian worms)

Dept of Agriculture and Food, Albany, W.A



How?

Vaccine culture system and bio-fermenter?

Ours is unusual,
it can walk and
is edible!



Advantages

1. Cost effective
2. Readily scaled-up!

Commercial Scale Barbervax Manufacture (Albany, Western Australia)



Commercial Scale Vaccine Manufacture



300g Haemonchus



Homogenisation



Antigen Extraction



Antigen Purification



Formulation, filter sterilising



1,000L Barbervax

Commercial Scale Vaccine Manufacture

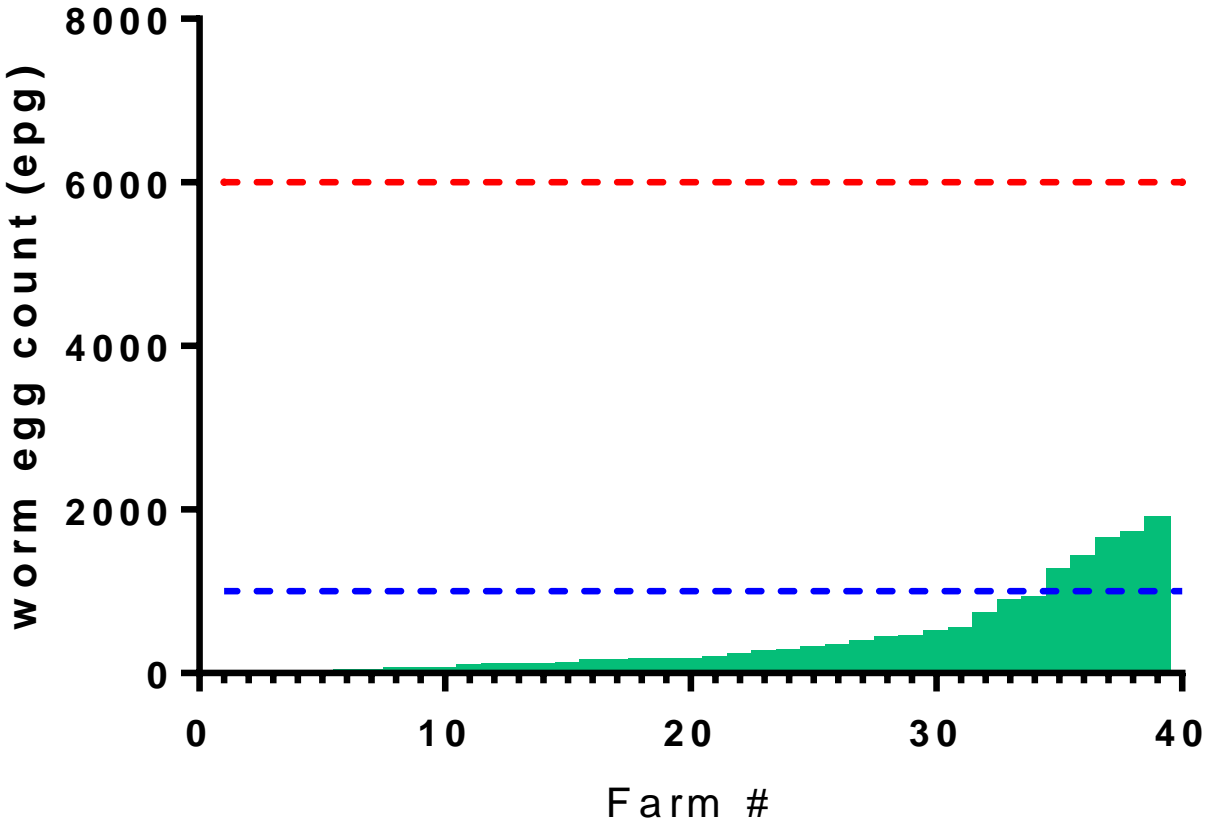


Sterile filling and finishing inside isolator

Expect to have
4 million doses
available in time
for 2016/17
season

Good Manufacturing Practice Licence 2011

Barbervax performance in lambs Jan to May



Testimonials

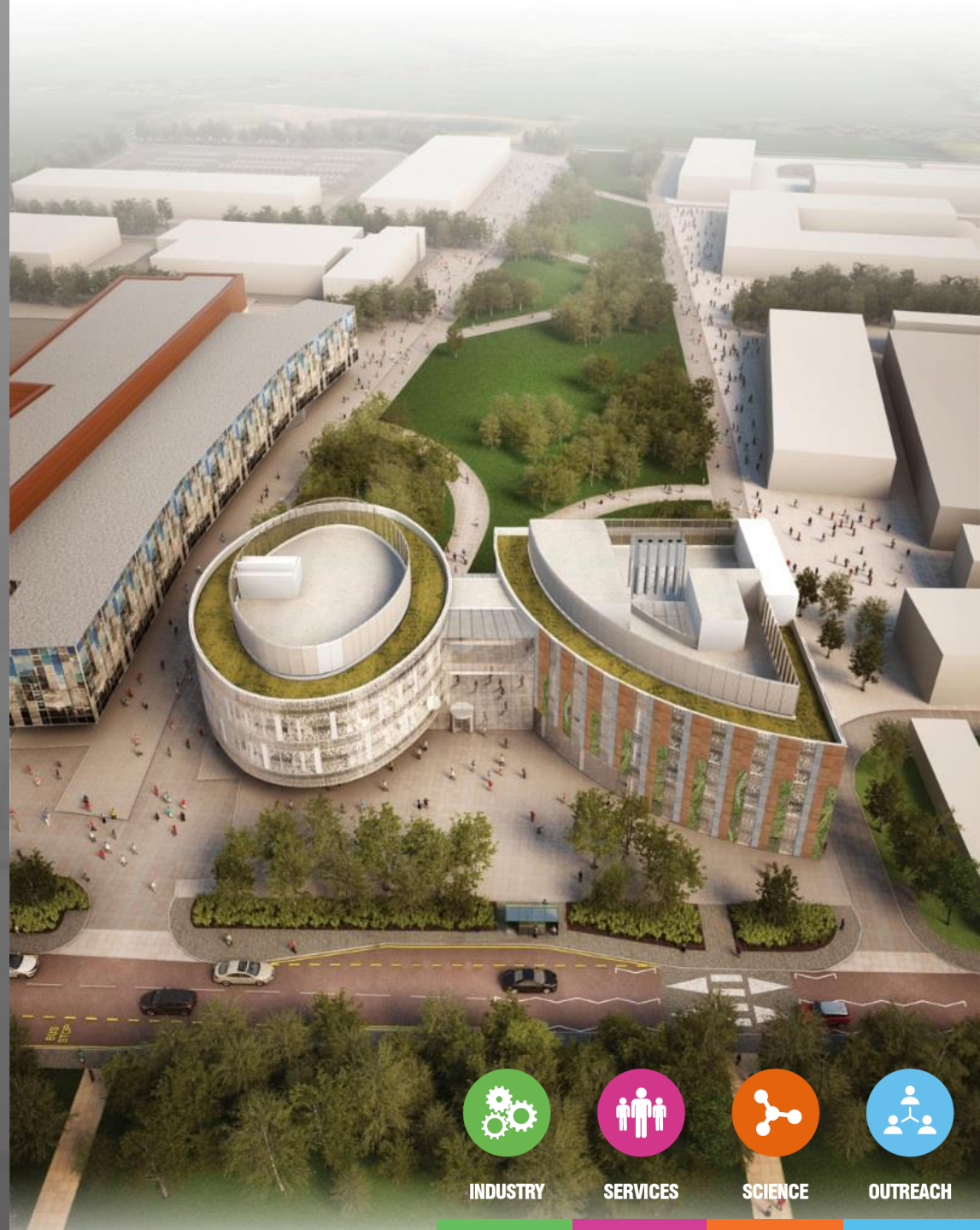
- *“We were very pleased with the action of Barbervax on our young sheep in this year”.*
- *“We are delighted with the first year results and will most certainly be using it again in Spring 2016”.*
- *“We have been using it in ewes and rams as you know to great results. Tell the scientists if they could just come up with a once year booster for all worms and fly strike....and make it rain”.*
- *“Just awesome results. We are very happy with your vaccine and have been telling anyone who will listen to us about it.”*

Where next?

- On track to make 4m doses for 2016 /2017
- Start exporting to South Africa?
- Start registration process in Uruguay / Brazil?



The business location of choice for companies undertaking strategic, commercial and collaborative research in the Animal and Veterinary Sciences; Agri Tech and One Health industries



THE UNIVERSITY of EDINBURGH
Easter Bush Campus



INDUSTRY



SERVICES



SCIENCE



OUTREACH

❑ European Centre of Excellence in Animal Sciences and Food Security



❑ Edinburgh recognised globally as

“... a world capital for livestock health and genetics ...” – Bill Gates, Nov 14



THE UNIVERSITY of EDINBURGH
Easter Bush Campus



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- ❑ £30 million flagship Roslin Innovation Centre and Campus Hub (Centre Building)
- ❑ Construction commenced Mar 2015 and due to complete Aug 2017
- ❑ University of Edinburgh (UofE)
- ❑ Biotechnology Biological Science Research Council (BBSRC)
- ❑ Scottish Government



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- ❑ An urgent window of time with:
 - *Growing middle classes*
 - *Increasing demand for meat, milk and eggs*
 - *The need to feed more with less*



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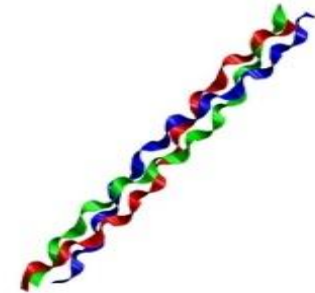
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Triple Helix+ Model

- An environment for **innovation**
- Enlightening culture
- Strong and visionary leadership
- Translation and convergent opportunities
- Business, academics, clinicians, students, government agencies and public – **all under the one roof**
- Impact – economic, cultural, environmental, health, public policy and societal on a local, national and **international** stage
- Ring-fenced business model with profits reinvested



- ❑ Focus on Livestock Improvement, Food Security and One Biology
- ❑ Dynamic environment with an industrial collaboration culture
- ❑ Co location with synergetic businesses and service companies
- ❑ Boost and significantly accelerate the innovation process from:
 - idea to product and service
 - student and researcher to entrepreneur
 - lab to market
 - trough to table
 - start up to growth company



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The Royal (Dick) School
of Veterinary Studies



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Easter Bush Campus



- ❑ Largest concentration of animal sciences in Europe
- ❑ Commercial and collaborative research opportunities
- ❑ Part of a co-locating, co-creating community at Easter Bush Campus
- ❑ Follow on space availability for growing companies
- ❑ Caters for different **tenant types** and different organisation types
- ❑ **'All-in'** stepped rental accommodation cost:
 - inclusive of services and utilities
- ❑ Support from **Central Services Unit (CSU)** on PAYG basis
- ❑ **Business development**, acceleration and service opportunities
- ❑ **Campus Hub** - for staff, students, public, tenants and visitors
- ❑ Good transport links

- ❑ Established companies; multi nationals; new and existing R&D strategic partners or Roslin/RDSVS/SRUC spin outs, spin ins, start-ups and scale ups categorised into different tenant types of:
 - ❑ ‘Incubate’ - company or organisation within its 1st three years of operation and on a short term, ‘easy in easy out’ occupancy
 - ❑ ‘Anchor’ - established company on a longer 5 year fixed term occupancy
 - ❑ ‘Partner/project’ - strategic collaborative partnership, joint venture or commercial research programme (non-entity) on either a short, medium or longer term basis
- ❑ No dominant tenant/tenant types i.e. neither to be occupying > 33% of the 41,000 square feet of lettable space



- ❑ Flexible office and laboratory space
- ❑ Open plan accommodation with quick, easy and secure sub-division
- ❑ Equipped to high standard providing bright and airy workstations
- ❑ Full height glazing with countryside views for 380 people (office) & 285 people (lab)
- ❑ Common access to meeting rooms, kitchen areas, showers, changing facilities and toilets plus local amenities
- ❑ Break-out space for collaborative working



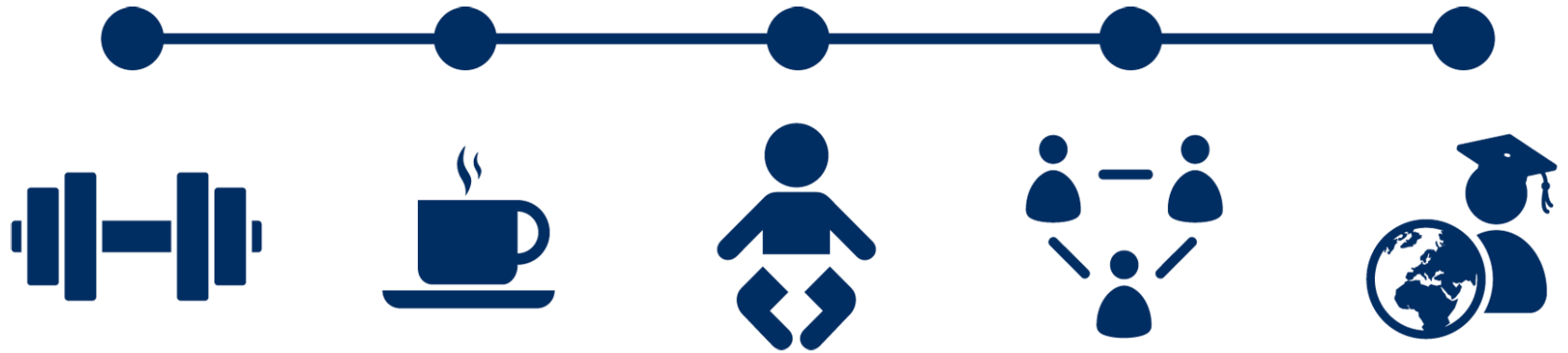
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Open plan and/or glass partitioning



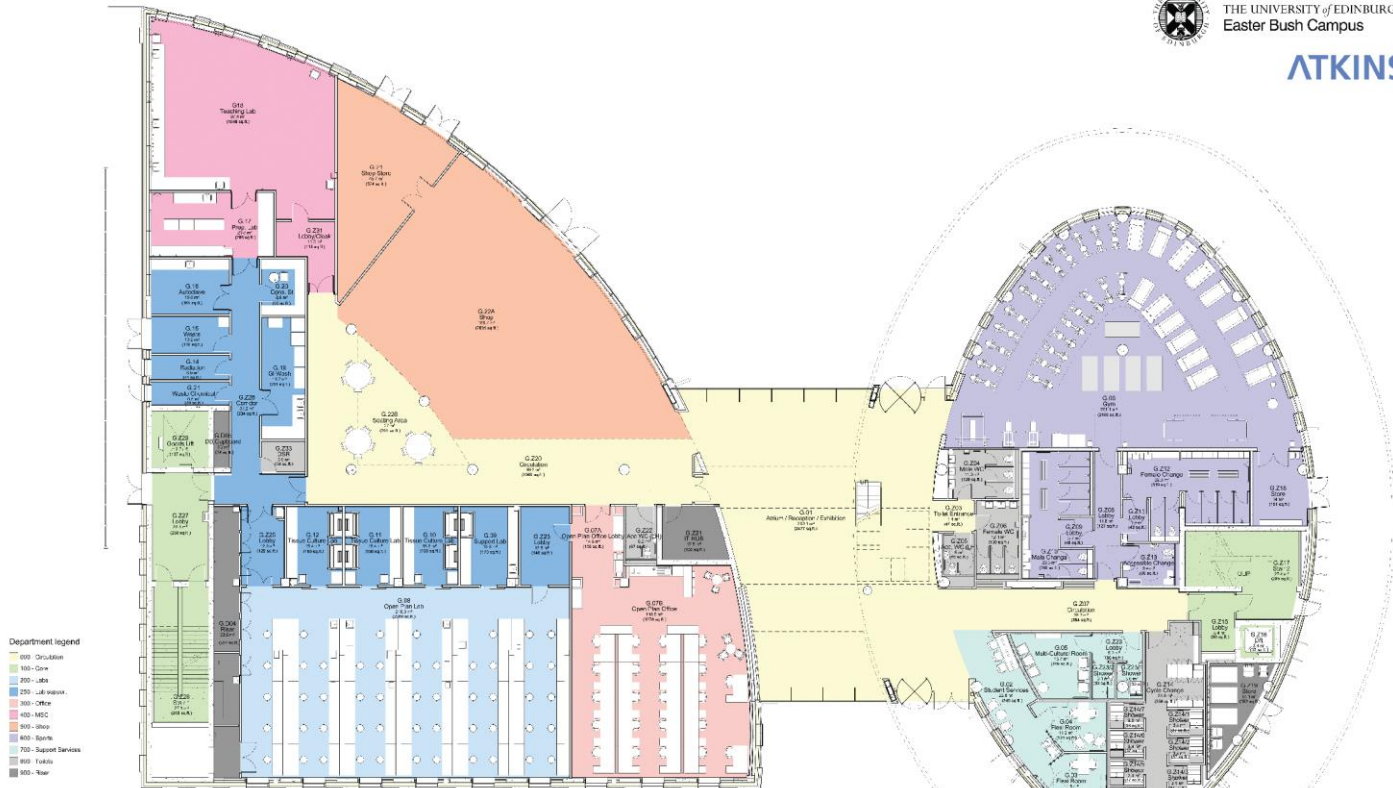
- Amenities include gym, shop, cycle changing & showers, Science Outreach Centre for public engagement, contemplation room and on site campus nursery



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Random Collisions - "Exchange Street"



Research Hotel?

Ground Floor Plan



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'All-in' accommodation cost

- ❑ Competitive and affordable 'all-in' cost
- ❑ *Easy in, easy out* 12 month occupancy agreement (incubate) or 5 year lease (anchor)
- ❑ Stepped rentals, £psf basis and/or '*rent a desk, rent a bench*' [POA]
- ❑ Basic utility costs included - heat, light, power & water service charges
- ❑ Cleaning plus ample car parking included
- ❑ Additional charge for Internet Connection to the University's high speed, high bandwidth JANET data network over dedicated fibre-optic cable via secure and reliable remote servers



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Easter Bush Campus



- ❑ Ready set up laboratory space with a wide range of shared facilities
- ❑ Fully serviced suites in a supported environment and full integration within the wider Campus infrastructure and access to scientific equipment and specialist facilities
- ❑ Secure building with swipe card access system and Bio Security
- ❑ Health & Safety with UofE Biological & Laboratory Safety compliance
- ❑ **Pay As You Go** Central Support Unit (CSU) for :
 - cold room, wash up/autoclave room, specialist waste handling
 - distribution of solutions and glassware to central storage areas
 - lab consumable service and communal weigh room
 - freezer management service



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Facilitated access to:

- ❑ Heads of the science divisions and academic group leaders
- ❑ Edinburgh BioQuarter for academic scientists, clinicians and patients
- ❑ UofE's College of Science and Engineering enabling collaborative development of new drugs, diagnostic tools and medical devices
- ❑ Wide network of business professionals; mentors; NEDs and investors
- ❑ Company growth opportunities incl. adjacent brown-field development



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Facilitated access to:

- Bio imaging/Cell sorting & Flow Cytometry Facility
- Proteomics Facility and Mass Spectrometry service
- Biological Research Facility
- The Centre for Comparative Pathology
- Edinburgh Genomics
- The Wellcome Trust Clinical Care Facility for Large Animals
- The National Avian Research Facility



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Open for business



- ❑ Open August 2017
- ❑ Roslin BioCentre currently full
- ❑ ‘Pop-up incubator’ next door at the Sir Alexander Robertson Building
- ❑ Already hosts **Greengage Lighting Ltd**, recently relocated from London and **Kajeka Ltd**, the Roslin Institute’s latest spin out company
- ❑ Strong evidence of demand with Heat Map of 100+ potential tenants

... *if you think this is a place for your business now or in the future*






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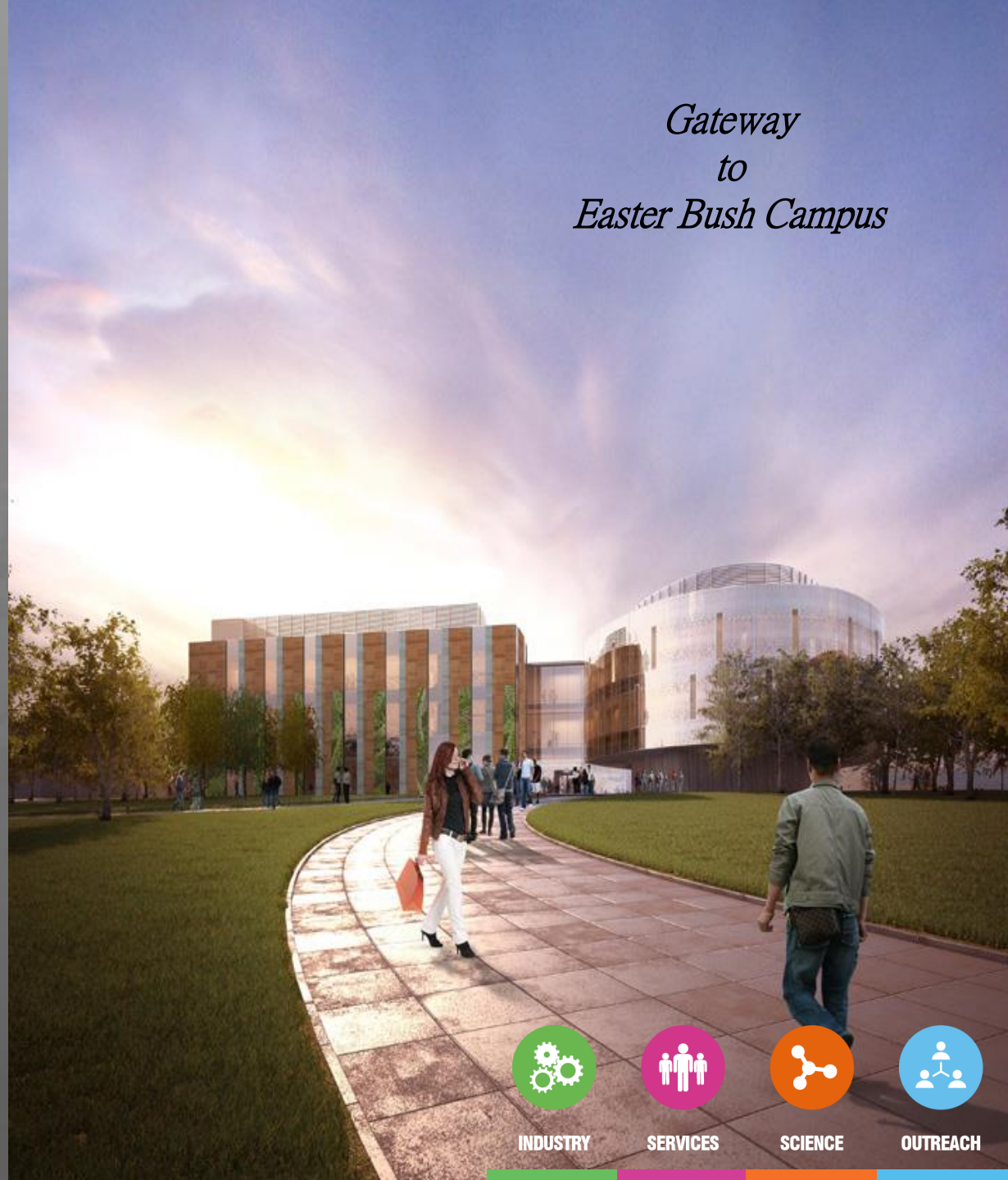
 @roslinnovation

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*Gateway
to
Easter Bush Campus*



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