Institution: Royal Veterinary College

Unit of Assessment: 6

1. Unit context and structure, research and impact strategy

In REF5a we defined our underpinning philosophy to encourage curiosity-driven research which benefits lives of humans and animals and set out our research and impact strategy to achieve this, by further developing our comparative, global, integrated and inter-disciplinary (One Health) approaches. Here, this strategy, as it relates to our main research programmes and groups, is described in detail.

To facilitate our research strategy, we recognise the need to develop cross-cutting skills and capacity to handle different types of large data-sets, combine, model and analyse these to generate and test hypotheses. The massive increase in capacity to capture data from all areas means data analytics skills development is essential for One Health research. Our broad strategic approach, progress and future plans for this are outlined below within research group narratives.

For all our research areas to have impact, we recognise the need to understand how our stakeholders will use the solutions we develop and whether these solutions will gain societal acceptance in the proposed context. Thus, involving stakeholders, policy makers, social scientists and ethicists at the appropriate stage is important for acceptable solutions to result. The partnerships and collaborations we have established to develop social science expertise, involving policy-makers and stakeholders are explained with examples within our research group narratives and in section 4.

Research Management Structure: Research programmes and Groups

RVC's academic resource allocation and management structure is detailed in REF5a. The Vice Principal Research and Innovation (VPR-I) leads the research mission and chairs Research Strategy Committee (RSC), which reports to the Academic Board recommending strategic investments and policy changes to enhance the research environment. Membership of RSC is detailed in REF5a. The 2 research programmes (retained from REF2014) have provided a successful structure with flexibility in research groupings supporting evolving areas.

Groups have overlapping interests and academics may be members of multiple groups. We have developed strength and capacity in disciplines that are applied to many research questions across our groups. Professional identity and discipline support networks are retained within academic departments. These include epidemiology, genetics and genomics, comparative pathology, immunology, animal welfare and ethics and veterinary education. Research specific to the latter

two areas is included in our return with each discipline as a group. The relationship between academic departments and the overlapping research programmes and their constituent groups is depicted in Figure 1:

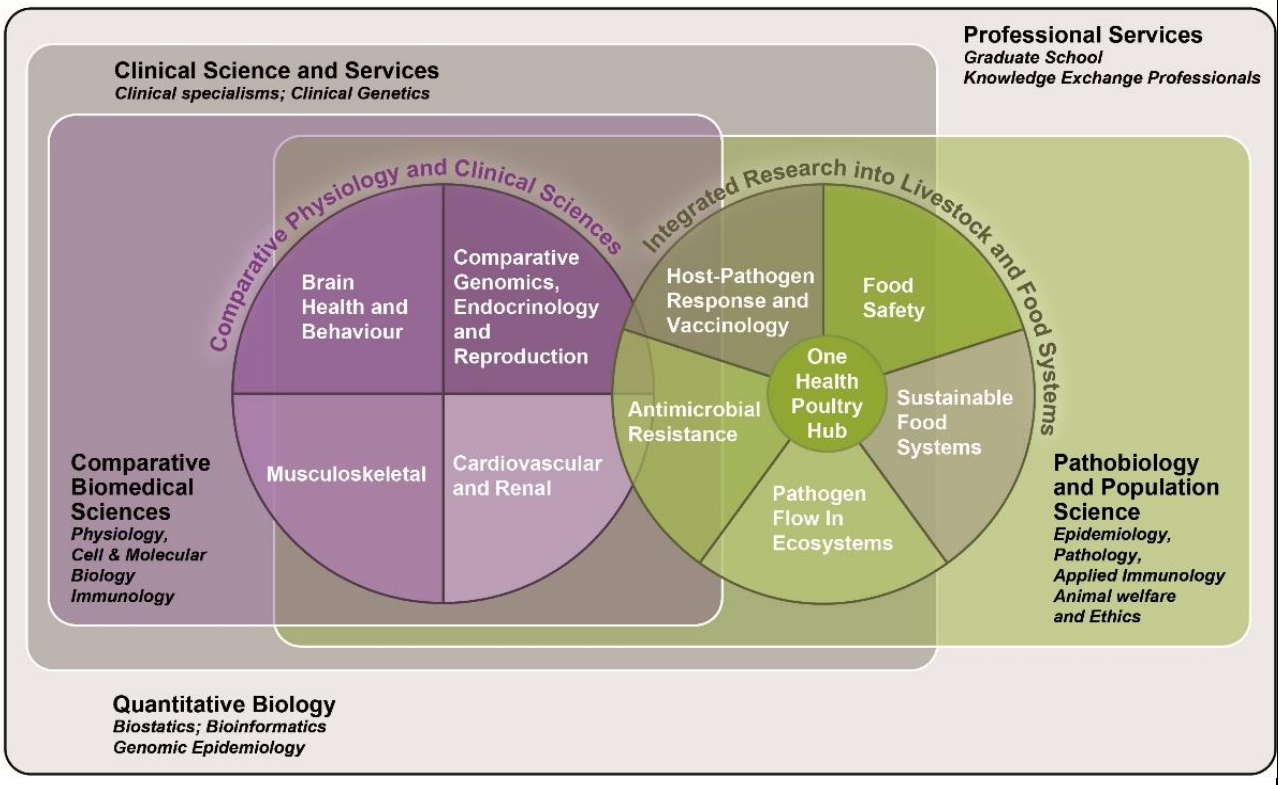

Figure 1: showing interaction between interdisciplinary research teams, Comparative Physiology and Clinical Sciences and Integrated Research into Livestock and Food Systems, and their relationship to academic departments and professional services.

Quantitative Biology strategy:

An important part of our research strategy that has progressed during REF2021, is to support and train our scientists in cutting-edge technologies to maximise use of their data. Our quantitative biology strategy encourages data scientists working across fields (from genome sequences (host, pathogen, microbiome) and metabolomics to population pharmacokinetics and complex simulation data modelling) to share new ways of working.

Strategic appointments have been made during REF2021 to enhance critical mass and progress quantitative biology skills across both research programmes. Support for quantitative biology has been a priority, building on the foundation of veterinary epidemiology established under Dirk Pfeiffer's leadership (1999-2016). Expansion of support beyond those trained in epidemiology occurred with Yu-Mei Chang's appointment (2009), a chartered statistician, dedicated to support researchers and PGR students. Capacity has been further enhanced in REF2021 with appointments in bioinformatics, **Dong Xia** (2017; from Liverpool University), clinical genetics

Androniki Psifidi (2017; from Roslin Institute) and mathematical modelling **Martin Walker** (2017 from Imperial College). Clinical genetics research fellow, **Marsha Wallace** (2020, from Oxford) leads bioinformatics pipeline development for complex diseases. During REF2021, our epidemiology capacity has been expanded and diversified by new appointments and a strategic partnership in genomic epidemiology with Oxford University (Zoology Department) providing expertise in pathogen genome evolution during disease outbreaks (Ecosystems Health Group). Expanded capacity to mine data acquired through Vetcompass™, RVC's system for accessing real-time data from primary care practices, now involving 1800 practices, provides significant opportunities for big data analytics. Appointment of **Dan O'Neill** (from RVC post-doc; 2018), dedicated to further Vetcompass™ development facilitates its application across groups to ask questions directly applicable to veterinary practice and pedigree dog health (in partnership with the Kennel Club). Parallel infrastructure investments in quantitative biology are described in section 3. Dr Chang leads this important strategic area and is a RSC member, ensuring investments continue to support researchers to maximise use of their data.

Future goals: Strategic investments made in this field will support our future goals defined in REF5a and detailed below. New strategic developments in Quantitative Biology for REF2026 will facilitate researchers to:

-apply artificial intelligence and machine learning to develop novel research and diagnostic tools (e.g. analysis of physical activity data in experimental dogs to detect treatment effects in muscular dystrophy);

-develop and apply natural language processing skills to extract data from Vetcompass™ and undertake spatial analyses to identify environmental factors contributing to disease patterns.

Research Programmes

Comparative Physiology and Clinical Sciences (CPCS)

CPCS is led by Dominic Wells, a translational scientist whose career has been dedicated to understanding the molecular basis of neuromuscular diseases and determining the appropriate models predictive of treatment success. His approach of integrating molecular, cell and developmental biology into whole animal physiology and pathology to understand the interaction between genotype and phenotype (including environment, diet and exercise) is one we strive to engender in CPCS researchers. The rationale for focusing on chronic diseases of modern lifestyle, where veterinary patients provide human disease models is explained in REF5a. Through Wells's leadership, ethical appropriate model selection, reproducibility and openness of animal experimentation are all emphasised.

Where appropriate veterinary patient use is part of our 3Rs strategy. VetCompass™ provides access to veterinary patient data at scale. Dedicated clinics, held within our referral hospitals,

recruit patients of interest (drug resistant epileptics; hard to regulate diabetics) supported by industry collaborations. Collaborations with charities (e.g. PDSA) provide access to common problems where referral is unnecessary or where early stage disease is not recognised (e.g. chronic kidney disease). Tissue and DNA archives linked to clinical databases are supported by appropriate infrastructure facilitating our comparative genomics strategy.

The 4 groups within CPCS have between 20-38 academics; combinations of basic scientists (cell and molecular biologists, whole animal physiologists), specialist clinicians and pathologists. Input from geneticists, epidemiologists and welfare scientists is obtained as appropriate. Common interests between groups are explored at the Programme Management Committee (PMC), ensuring synergistic expertise is exploited. Subgroups have emerged (in musculoskeletal biology) around shared facilities but retain pre-clinical–clinical connections and translational approaches. Clinical research outside the focus of these groups is supported within the programme.

a. Musculoskeletal (MSK) biology

Healthy ageing depends on identifying ways of sustaining pain-free mobility with adequate muscle strength into old age. Comparative locomotor biology of animals is fundamental to how we teach structure and function. We have sustained world-class MSK biology research over 35 years, founded on basic science of how the skeleton adapts to strain, what constrains muscle performance and how tendons contribute to athletic performance. As outlined in REF2014 future plans, application of mathematical and physical scientific principles to model and understand the MSK tissue interactions with each other and the environment, using ever-increasingly sophisticated measurement techniques, have underpinned advances made. Translational research is strong, with innovations being transferred to the clinic for lameness diagnosis, treatments (tendon cell therapy, electrical stimulation and novel surgery for laryngeal paralysis) with novel treatments for muscle disease (gene editing), osteoporosis (partnership with Haoma Medica) and imaging cartilage defects (Raman spectroscopy) in the pipeline. Bioinspired robotics is an important translational element of the Structure and Motion Lab's (SML) work. The MSK Biology Group has 37 academics, with 8 to16 academics in subgroups described below.

Structure and Motion Laboratory led by Alan Wilson FRS was established in 2004 and has trained 50 talented researchers who subsequently progressed into independent research positions. During REF2021, SML academics held five European Research Council grants, a Wellcome Senior Research Fellowship (SRF) and responsive mode grants from BBSRC. US Air Force and Defence Science Technology Laboratory (DSTL) fund their bioinspired unmanned autonomous vehicle research. Developing interest in animal flight control systems led to recruitment of **Andrea Gaede** (2020; from University of British Columbia). Within 3 months of finishing his ERC Starting Grant, Richards was awarded a Wellcome Investigator award (2019-2024). Innovation is encouraged with laboratory personnel building equipment. They have

pioneered physiological measurement in free-moving animals in remote areas, using these measurements to undertake curiosity-driven research. Application of physiological principles constraining and controlling animal movement to robotic design is an overarching SML goal.

Bone, Tendon and Joint Laboratory is led by Andy Pitsillides, who has refined Lance Lanyon's bone-loading model to expose joints to increased strain, mimicking the wear-and-tear of over-use. His ability to combine molecular and cell biology, study cross-talk between skeletal tissues (bone, vasculature and cartilage), analyse histomorphometry and microCT data combined with *in vivo* measurements of strain and function (gait analysis) makes him a leader in bone biology. With collaborators he has developed a paradigm-shifting hypothesis that changes in bone shape predetermine age-related osteoarthritis onset. His partnership with Haoma Medica, built on intellectual interactions with CSO Stephen Hodges (RVC Honorary SRF) is yielding promising results around novel osteoporosis and osteoarthritis treatments (patent application filed). Mechanisms by which cartilage transitions to bone are poorly understood and this knowledge underpins bone repair and is relevant to joint regeneration. RVC is a partner in the CarBon Marie Sklodowska-Curie ITN, which addresses this knowledge gap.

Bone pain and fracture repair are areas where basic science (led by Chenu) feeds into translational research. Partnership with Transpharmation, (Neuropharmacology SME) within a multi-institutional Marie Sklodowska-Curie ITN will ensure RVC becomes established in the bone pain field. RVC-trained orthopaedic specialist **Richard Meeson** pursued PhD training at UCL (MRC Fellowship), developing methods of mobilising endogenous stem cells to improve fracture repair. Meeson has returned to lead clinical orthopaedics and develop regenerative medicine translational research.

Building on pioneering use of autologous stem cells for equine tendon injuries, a Stem Cell Centre (SCC; infrastructure funding from Hertfordshire LEP) has been established. The SCC, which has Veterinary Medicines Directorate approval, is led by Jay Dudhia, offers services for veterinary practices and undertakes clinical trials to provide the evidence-base for cell therapies. New appointee, **Scott Roberts** (UCB Pharma; 2019) adds capacity in fundamental science underpinning skeletal regenerative medicine.

The quality environment created for MSK biology attracts externally-funded research fellows. Under Dudhia's and Pitsillides's mentorship, **Chavaunne Thorpe** (Versus Arthritis Fellow; 2016-2021; appointed to a lectureship 2020) studies the interaction between interfascicular matrix and tendon progenitor cells, novel basic biology underpinning tendon repair. This adds a new dimension to Roger Smith's (Clinician Scientist) and Dudhia's (Matrix biologist) work, who lead

this field. They are part of the Tendon Therapy Train consortium (EU Marie Sklodowska-Curie ITN) with partners in academia, industry and private practice.

Neuromuscular biology: Dominic Wells established this sub-group in 2010. The development of Clinician Scientist Richard Piercy over this period has been remarkable. Building on Wells's expertise of mouse Duchenne muscular dystrophy (DMD) models and capitalising on his discovery of a canine patient with DMD (mutated splice site in dystrophin's exon 50), with Wellcome funding Piercy has developed the E50 DMD dog model. This is being used to develop novel treatments (gene editing, exon skipping) funded by Human Pharma. He involves expertise from the SML, cardiologists and animal behaviourists to fully characterise the model's phenotype, and uses activity monitoring to assess treatment effects. Clinical Research Fellow and neurology specialist **Abbe Crawford** has secured Academy of Medical Sciences (AMS) funding to characterise the model's brain phenotype with a view to assessing novel treatments.

In studying another naturally-occurring disease, recurrent laryngeal nerve neuropathy, Piercy has teamed up with equine surgeon, Justin Perkins, medical devices company Med-el Ltd., and Cornell University to devise ways of encouraging muscle regeneration through electrical nerve stimulation. Recognition of their skills in peripheral nerve physiology has led to collaboration with David Holder (UCL, Medical Physics & Engineering) and Galvani Ltd., developing large animal models for bioelectronic medicine, initially working to optimise the autonomic nerves which have the greatest immunomodulatory effects. They work with immunologist Dirk Werling to understand the mechanism(s) underlying these remarkable responses.

RVC's growing reputation for translational regenerative medicine has attracted clinician scientist **Nicolas Granger** (Bristol, 2017) to lead an EPSRC-funded project (with UCL Medical Physics). Granger, a neurosurgeon, is devising pre-implantation treatments of oligodendrocytes, to improve efficacy in spinal cord injury treatment.

Principal Achievements:

-Described wing kinematics of mosquito flight, defining novel elements dependent on wing rotation not velocity

-Modelled energetic efficiency of wildebeest muscle (from direct fibre measurements) to explain how they overcome thermoregulatory challenges in hot arid habitat

-Devised synchrotron X-ray tomography combined with mechanical loading at nanometric precision for *in situ* imaging, enabling a detailed view of OA progression in different joint components as it evolves

-Proposed mechanism of fascicle sliding and rotation to explain age-related tendonopathy

-Defined the natural history of a new DMD dog model

Future plans: Building on strong foundations of fundamental MSK science, during REF2027 we will continue to exploit that knowledge to benefit society. For example we aim to:
-Use knowledge of insect flight physiology and navigation systems in unmanned aircraft design (US Airforce/dstl; 2019-2022) and to control insect disease vectors (RVC-Pirbright studentship; 2021-2024)
-Understand how age-related changes in muscle influence neuromuscular control of reaching (Wellcome; 2019-2024)
-Explain how growth plate cartilage dynamics and joint biomechanical functionality are linked to provide new mechanistic understanding of joint health and pathology determinants
-Test novel DMD therapies using the mdx mouse and delta-E50 MD dog model (Industry funding; 2017-2022)

b. Cardiovascular and Renal Biology:

Caroline Wheeler-Jones, an expert in endothelial cell signalling and angiogenesis leads this group. There are strong links to other CPCS groups through shared interests in vascular calcification (with Bone Biologist Isabel Orriss), circulating endothelial progenitor cells (fracture repair cell therapy; Meeson/Roberts) and ischaemic neonatal brain damage (Brain Health & Behaviour; Thornton and Stolp). The core scientific research is built around Wheeler-Jones's expertise. Recent recruits include **Caroline Pellet-Many** (from UCL, 2018) who focuses on neurophylins' role in angiogenesis bringing expertise in zebrafish models of cardiovascular regeneration. BHF fellow, **Christina Warboys** (from UCL; 2019) will transition into a lectureship bringing expertise on flow patterns and endothelial cell signalling, relevant to atherosclerosis research, complementing Wheeler-Jones's work on dietary lipids. Finally, **Matthew Gage** joined (from UCL in 2019) bringing expertise in atherogenesis and angiogenesis related to insulin dysregulation and diabetes, also relevant to the Comparative Genomics, Endocrinology and Reproduction group.

Wheeler-Jones has a strong track-record of fostering collaboration across disciplines by working with clinicians. She currently co-mentors (with Piercy) HBLB Fellow (2019-2022) **Liz Finding** (RVC-trained) who is exploring the role of exosomes in exercise-induced muscle angiogenesis. Ischaemia is proposed as a major factor contributing to feline kidney damage. RVC is the leading veterinary institute undertaking feline chronic kidney disease (CKD) research. Wheeler-Jones's cell biology expertise has been harnessed to establish feline tubular epithelial and cortical renal fibroblasts cell culture, allowing study of cell responses to hypoxia (collaboration with Veterinary Pharma).

The geriatric cat clinic, established by Elliott, recruits CKD cases through RVC's primary care practice and the PDSA. This research has received 28 years of industry support and continues to generate novel insights and train high quality clinician scientists. The focus is on bone-mineral disturbances and hypertension. **Rebecca Geddes**, a graduate of this programme is a new recruit (2019). She won a Clinician Scientist Fellowship to focus on research in collaboration with the Wellcome Centre for Human Genetics (WCHG), Oxford University and secured AMS funding for urinary stone disease work. Rosanne Jepson's research into genome influences on CKD progression and hypertension with QMUL BHF Professor, Patricia Munroe is yielding interesting results. The cat clinic's research has supported commercialisation of drugs, diets, diagnostic tests and informed clinical guidelines (see Feline CKD impact case study (ICS)).

RVC is renowned for clinical cardiology research. Adrian Boswood has used charity clinics to recruit degenerative mitral valve disease (DMVD) cases to longitudinal study, identifying predictors of progression in preclinical-stage patients to target treatment without specialist imaging. Continuous funding for 16 years has established a unique resource. Boswood has teamed up with Vetcompass™ to ensure his research generalises to primary care practice. His skills are sought after by industry. His design of the EPIC study is highly regarded and underpins our DMVD ICS. Boswood's research could select patients for surgical valve repair, a procedure pioneered by Brockman (specialist cardiac surgeon) making RVC the first centre in Europe or the US offering this.

Cardiologist David Connolly combines cell biology, supported by Dudhia (cell isolation and culture) and Werling (flow cytometry and immunology), and clinical research. He collaborates with Professor Terracciano at Imperial College using induced-pluripotent stem cells to investigate molecular mechanisms of feline hypertrophic cardiomyopathy (fHCM) and canine cardiospheres, hypoxia pre-conditioned, in a proof-of-concept trial as a novel treatment for dilated cardiomyopathy. His work aligns with RVC's regenerative medicine strategy where veterinary patients benefit from proof-of-concept work for human medicine. His fHCM research is complemented by that of Luis-Fuentes, which has defined the prevalence and risk factors for progression of fHCM, changing clinical practice to use limited echocardiography and biomarkers to identifying high risk cases (see fHCM ICS).

Principal achievements:

-Defined the roles of neurophilins in cardiac regeneration

-Determined that disturbed flow induces endothelial cell senescence via p53-p21-dependent pathway

-Demonstrated the importance of LXRα phosphorylation at S196 in atherosclerotic plaque development

-Identified plasma FGF23 and magnesium as novel survival and progression predictors in feline CKD

-Devised an algorithm to accurately identify dogs in B2 stage of canine DMVD without the use of echocardiography

Future plans: We will support the development of 3 ECR endothelial biologists into research leaders, facilitating application of their science to regenerative biology across systems of interest to CPCS. Using our developing canine and feline genomic pipelines to understand the genetics of complex diseases, such as CKD, DMVD and fHCM, we will exploit cell culture models, incorporating single cell transcriptomics and gene editing to explore pathophysiological mechanisms.

c. Brain Health and Behaviour

As one of our REF2014's future plans, this group has developed to a critical mass of 20 academics. Its evolution reflects a longstanding interest in canine epilepsy and recognition that canine idiopathic epileptics also exhibit behavioural abnormalities which improve on dietary medium chain triglyceride supplementation. This work, led by clinician scientist Holger Volk (Category C – promoted to Department Chair, Hanover) and animal behaviourist **Rowena Packer** (BBSRC Future Leaders Fellow; RVC-trained) underpins an ICS. Volk leaves a legacy of research-competent neurologists (**Beltran**, **Crawford, Whittaker** and **Fenn**).

The basic science underpinning neuronal resilience heavily depends on the cells' ability to remove ageing, malfunctioning mitochondria. Campanella (ERC Advanced Grant, 2019-24) studies mitophagy, asking how mitochondria and nuclei communicate. He works with developmental neurobiologist and group leader Claire Russell, who focuses on zebrafish lysosomal storage diseases models, exhibiting neurodegeneration and epilepsy.

Three neuroscience recruits increase our capacity to understand healthy brain functioning and ageing. **Claire Thornton** (2018, from KCL) focuses on mitochondrial protein optic atrophy-1 in neuronal ischaemic damage. She works with **Helen Stolp** (2017, from KCL), a pharmacologist interested in perinatal brain ischaemia's effect on neuronal development. **Patrick Lewis** was appointed to Neurosciences Chair (2020, from Reading), a new basic neurosciences leadership position complementing our clinical capacity. Lewis, a biochemist with expertise in mitochondrial protein-protein interaction, focuses on neurodegenerative pathways in Parkinson's disease.

In 2018, Merck established a group studying neuronal resilience in the London Biosciences Innovation Centre (LBIC), a step toward relocating R&D to London. RVC and Merck co-fund a post-doc (with Campanella) to establish collaborations. Arrangements have been made for shared equipment access.

Integrating animal behaviour science into major research projects undertaken by BHB scientists is a strategic goal. **Maria Diez-Leon's** appointment (from Guelph, 2017), expert in early-life influences on behaviour, increases our capacity to achieve this. Diez-Leon is analysing DMD dog behaviour with Crawford. Experienced welfare scientist, **Christine Nicol** (from Bristol, 2017) provides mentorship to our early-career welfare scientists. Objective assessment of veterinary patient behaviour is critical in assessing subjective phenomena (e.g. pain and nausea), which are important clinical research goals supported by welfare scientists.

Principal Achievements:

-Defined sub-cellular pathways involved in mitochondrial quality control and mitophagy

-Demonstrated that alterations in mitochondria-shaping proteins occur early in the pathogenesis of neonatal ischaemic brain injury

-Identified behavioural abnormalities that accompany canine epilepsy and assessed their response to dietary therapy

Future plans: We will encourage collaboration between basic scientists, animal behaviourists and clinical neurologists to use veterinary patients as human disease models. To support this we have funded the establishment of a companion animal brain bank and are co-funding the joint clinical and research Translational Medicine Centre to provide 3T-MRI facilities. Specific research goals are to:

-Define the molecular signalling axis for communication between nuclei and mitochondria in health and disease (ERC, 2019-2024)

-Determine whether protecting OPA1 integrity following hypoxia-ischaemia provides additional neuroprotection for infants where therapeutic hypothermia alone is inadequate (MRC; 2020-2023)

-Define mechanistic impact of LRRK2 upon progression across Parkinsonian disorders (ASAP; 2021-2024)

-Define cellular and functional consequences of brain dystrophin deficiency and develop strategies to restore its expression

d. Comparative Genomics, Endocrinology and Reproduction

Upskilling researchers in genome data-analysis is an important institutional strategy impacting both research programmes. New appointments to support this quantitative biology strategy were discussed above. These build on Larkin's appointment (REF2014) whose world-leading research into chromosome evolution has broad comparative genomics implications. To make full use of veterinary patients as human disease models, we have established systematic phenotype data capture processes coupled with DNA archives, enabling phenotype to genotype matching. To capitalise on this institutional strategy, we appointed Clinician Scientist, **Lucy Davison** (2017 from

Cambridge), a leader in this field, and established a strategic partnership with the WCHG (Oxford University). Within 6 months of her appointment, **Davison** won an MRC Clinician Scientist Fellowship (2018-2023). She studies the interaction between genes and environment in complex diseases and, in particular, the immunoregulatory *dexi* gene and the microbiome influence on mouse diabetes models and canine diabetic patients (publications delayed by Covid-19). Davison, group leader, is an internal medicine specialist who, supported by Psifidi, inspires clinicians to use cutting-edge functional genomics.

Whilst there are some well characterised veterinary monogenetic disorders, the real challenge is to understand genomic influences in complex diseases, to inform prognosis and provide individualised treatment. Working with RVC research fellow **Wallace**, Davison has established data analysis and processing expertise, developing a pipeline for prioritising important disease-associated variants within whole genome sequences. This pipeline is being adapted for other diseases and species and will become a foundation for future clinical research within CPCS. Davison also pioneers the use of single-cell transcriptomics (10X Genomics).

Endocrinology exemplifies the value of the comparative approach. Whilst dogs are most likely to develop type-1 diabetes, obese cats and ponies are insulin-resistant and cats develop type-2 diabetes. **Ruth Gostelow** (RVC-trained; 2016) is a clinician scientist who works to advance insulin-resistant diabetic cat diagnosis and management. Rob Fowkes, an endocrine physiologist, studies somatotroph regulation and collaborates with clinicians studying comparative pathophysiology of growth hormone-producing tumours, a treatable cause of feline diabetes (discovered at RVC). Insulin dysregulation in ponies is strongly linked to laminitis risk. Clinician scientist Menzies-Gow leads work on endocrinopathic laminitis with nutritionists from Waltham. Their intriguing finding that reduced circulating concentrations of adiponectin (adipocyte-derived hormone) is a strong predictor of incident laminitis has led to a new prognostic test to assist in laminitis management.

Genomic approaches are applied to reproduction, a long-standing RVC research strength under Claire Wathes's (Category C, retired 2019) leadership. Her EU-funded work with Fouladi and Werling into genomic contributions to dairy cattle disease resistance and infertility is generating significant outputs that will influence breeding strategies globally. Similarly, DeMestre works with the thoroughbred breeding industry on genetic influences on early pregnancy losses.

Principal Achievements:

-Discovered that avian genomes show a high degree of evolutionary stasis, but that pan-avian genomic diversity co-varies with adaptations to different lifestyles and convergent evolution of traits

-Characterised the chromosomal rearrangements leading to evolution of ruminants
-Demonstrated that disrupted dexi-expression speeds onset of diabetes in non-obese diabetic mouse model by changing the microbiome

Future plans: We will build on Davison's expertise to establish a leading centre for comparative genomics of complex diseases, where companion animals are used as human disease models. This will capitalise on our internal medicine expertise, collaboration with human medicine and application of whole genome sequencing data and subsequent follow-on genotyping technologies, such as Neogen array-based and TWIST sequence-based custom typing, adapted for disease and species. Fundamental understanding of chromosome evolution will continue to be exploited to inform livestock and poultry resilience to disease and climate change.

Integrated Research into Livestock and Food Systems (IRLFS)

The strategy underpinning IRLFS, and the global challenges it addresses are explained in REF5a. Here we explain in-depth the partnerships we have formed, the rationale for new appointments and detail major externally-funded initiatives supporting our work for the next 5 years.

The IRLFS programme involves 65 academics. It is co-ordinated by new recruit **Nicola Lewis** (2018, from APHA/Cambridge Zoology), a veterinarian and virologist who studies influenza A virus ecology and evolution in multiple hosts, evaluating the public health risks these pose. Nicola replaces Fiona Tomley as programme lead. Tomley now focuses on leading the UKRI GCRF One-Health Poultry Hub.

Success in tackling real-world challenges requires interdisciplinary approaches and strong academic and non-academic partnerships. UK academic partnerships were formalised, with the creation of the London International Development Centre (LIDC; 2007), funded by HEFCE. This partnership remains strong with 4 founding partners (RVC, LSHTM, SOAS, and UCL Institute for Education) and new associates, QMUL and City University adding breadth of disciplines and international networks. Leadership of LIDC is critical; providing strategic direction for interdisciplinary working. **Claire Heffernan** (2017, from Bristol) succeeded director Jeff Waage. Heffernan is Professor of International Development at RVC. A veterinarian with expertise in social sciences, she previously led interdisciplinary research centres addressing sustainable development goals at Reading and Bristol. Claire is a superb appointment for RVC/LIDC and combines this role with leading the UKRI GCRF Action Against Stunting Hub (2019-2024).

As relationships develop between academics across different disciplines, areas of mutual interest emerge leading to institutional agreements facilitating wider working relationships. This is the case

with Oxford Zoology, through **Oliver Pybus's** involvement in Influenza research; his skills in studying rapid pathogen evolution, particularly viruses, during disease outbreaks, complement other RVC Influenza researchers. RVC signed an agreement with Oxford Zoology for Pybus to hold a joint appointment (2018-2023) and exploit areas of mutual interest. Pybus's appointment supports development of bioinformatics skills at RVC, establishing genomic epidemiology as an underpinning science for infectious disease research.

Translation of research into policy is vital for successful implementation of solutions resulting from research. Pfeiffer's international reputation and networks established important policy-maker partnerships. RVC became an FAO Veterinary Epidemiology Reference Centre (2012), a designation renewed until 2024. In 2015, RVC entered a 2-year agreement with APHA to provide leadership for Epidemiological Sciences; this was extended resulting in the award of a joint OIE Collaborating Centre in Risk Analysis and Modelling (2019-2024), recognition of RVC's international reputation for risk analysis and its role in informing policy.

Working for sustained periods with partners from low- to middle-income countries (LMIC) is vital to understand cultural and societal influences on livestock and food systems and to build the trust needed to deliver excellent science. External funding stimulates these partnerships which RVC has sustained over 10-15 years, particularly in South and South-East Asia and Africa. For example, a BBSRC International Partnering Award (2008) and BBSRC/DfID CIDLID programme (2010) funded a partnership with Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, led by Fiona Tomley working on chicken coccidiosis. An extended network of partners and research into poultry gut health was further supported by the BBSRC/DBT FADH call (2013), partnerships which are now sustained through the RVC-led UKRI GCRF One-Health Poultry Hub (2019-2024). Similarly, three institutions in Bangladesh (CVASU, BLRI and IEDCR) were partners in the ZELS BALZAC project (2014-2019) and are now part of the Poultry Hub. Likewise, partnerships in Senegal with University Cheikh Anta Diop de Dakar, funded under ZELS (Schistosomiasis; PI Webster), have been sustained through the UKRI-GCRF Action Against Stunting Hub.

Furthermore, OIE funded an RVC-Jordan University of Science and Technology (JUST) partnership to develop their veterinary sciences curriculum and facilitate exchange of masters students (2015-17). The relationships established with JUST scientists, facilitated the award of a MRC GCRF Foundation grant (2017-19) on MERS virus in camels followed by a 3-year programme grant (MRC, £2M; 2021-2024), which aims to develop acceptable public health interventions that reduce MERS risk.

Thus, the IRLFS programme fosters collaboration between academics working with populations and ecosystems (epidemiologists, public health, economics and wildlife experts), those studying at herd/individual animal and molecular level (clinicians, pathologists, immunologists, vaccinologists, reproduction and welfare scientists), and microbiologists focusing on key pathogens. Most projects are challenge rather than discipline-led and whilst we describe constituent parts under five groups, there is much cross-talk fostered by the PMC with most academics belonging to multiple groups.

UKRI GCRF One-Health Poultry Hub is an excellent example which includes academics from all IRLFS's groups. This interdisciplinary Hub will influence RVC's research strategy for the next decade, with 8 researchers named as co-investigators and others making significant contributions. Hub UK partners are LSHTM, Oxford Zoology, IDS Sussex, Pirbright, Chatham House and APHA, with LMIC partners in India, Sri Lanka, Vietnam and Bangladesh. The real-world challenge for this Hub is: 'To achieve sustainable global intensification of poultry meat and egg production whilst reducing risks to human and animal health and welfare'. Poultry products are the biggest global animal protein source for humans. A major challenge is to achieve sustainable expansion whilst reducing risk from: 1) epidemic Avian Influenza; 2) antimicrobial resistance; 3) foodborne zoonoses; 4) disruption of the chicken gut microbiome, leading to increased pathogen carriage. Significant reductions in human and animal health risks require holistic interventions (technical, behavioural and regulatory) designed for, and implemented across, all production system levels. By tracking microbe transmission at genomic level through well-mapped poultry production and distribution networks in 4 countries, each at differing stages of intensification, a deep understanding of epidemiological risk factors, including those that govern decision-making and human behaviours will result. This will identify the riskiest factors and behaviours for targeted intervention. By working with local and national stakeholders, we will test, monitor and evaluate interventions designed to reduce antimicrobial usage and pathogen transmission and increase productivity, food safety and security.

The Hub exemplifies the IRLFS programme's ethos, namely: to solve problems that limit livestock productivity, our research must provide tailored solutions that take account of geographical, population, ethnic and socio-economic conditions. Their implementation needs support through partnerships with stakeholders, government and industry. This ethos runs through the 5 overlapping groups described below. The appointment of **Tony Barnett** (2020, from LSHTM), who leads the Hub's social science work package, provides mentorship for ECRs.

a. *Pathogen flow in ecosystems*

This group studies factors driving pathogen evolution and flow between environments, transmission vectors/intermediate hosts, animals (wild/domesticated) and humans. **Joanne**

Webster (2014, from Imperial College) leads the group. Her novel work on schistosomiasis, a neglected tropical disease of human and animal health importance, has demonstrated zoonotic human and animal schistosome hybrid formation and modified WHO future control strategies, taking account of livestock and wildlife's roles in human schistosomiasis epidemiology and control (see Schistosomiasis ICS). Schistosomiasis afflicts 250,000,000 of the world's poorest people. **Martin Walker** mathematically models transmission of neglected tropical (parasitic) diseases (NTDs), including schistosomiasis. Walker's skills add a new dimension to our Quantitative Biology strategy. He also works on drug resistance in helminth NTDs through collaborations fostered by RVC's membership of the London Centre for Neglected Tropical Diseases.

Genetic evolution facilitating transmission between species is a feature of avian influenza (AI). RVC's AI research was established by Pfeiffer following re-emergence of highly pathogenic AI (H5N1; 2003), and contributed to an FAO-funded international consortium, producing important statistical risk models informing control measures in SE Asia. This work, increasingly led by Guillaume Fournie (Pfeiffer protégé), has focused recently on poultry in Bangladesh (ZELS BALZAC project) and now in the One-Health Poultry Hub across Asia. Capacity in influenza research increased with the appointments of Lewis and Pybus (see above). Through an APHA strategic partnership, Lewis remains Deputy Director of OIE/FAO International Reference Laboratory (IRL) for AI, swine influenza and Newcastle Disease. Ian Brown (IRL Director, APHA) holds an RVC honorary post (2018-2021). Lewis and Pybus provide a new dimension of research leadership into emerging viruses of animal and human health significance. RVC is a base partner in one of only 3 NIH-funded Centres of Excellence in Influenza Research and Response, led by University of Pennsylvania (2021-2028), an indicator of its established international reputation in this important field.

Peste des Petits Ruminants (PPR) is another virus where wildlife play an epidemiological role. RVC has collaborated with the Pirbright Institute on PPR since 2004. Richard Kock leads wildlife PPR research, investigating their role in its spread from Africa into the Middle East and Asia, where its impact on small ruminants, upon which the livelihoods of pastoralists depend, is serious. Kock's work, funded initially by an ERA-Net ANIHWA grant and subsequently by GCRF Foundation (2018-20) and Global Research Translation Awards (2019-21), is informing the FAO PPR Global Eradication Plan as proposed in REF2014 (Saiga ICS). **Bryony Jones**, an FAO veterinarian involved in Rinderpest eradication, joined Kock's team (as researcher co-investigator) after completing her PhD on PPR. In 2019, Jones won an RVC strategic fellowship to lead PPR research in partnership with ILRI.

Julian Drewe leads wildlife-livestock disease transmission research studying the social structure of meerkats and badgers, where TB persists. He also assesses wild boar reservoirs as disease

risk for the UK pig population. Drewe's first PhD student, **Stuart Patterson** (2018) has been appointed to a lectureship, increasing our wildlife health expertise.

Principal Achievements:

-Quantified swine influenza viruses antigenic diversity on an multi-continental scale

-Demonstrated that hybrids originate in humans via zoonotic spill-over from livestock populations, where schistosomiasis is co-endemic, informing WHO Schistosomiasis control guidelines

-Documented PPR as the cause of mass mortality of Mongolian Saiga, informing wildlife inclusion in National PPR strategies and FAO Global eradication plan

Future goals: Having made strategic appointments with skills in pathogen genomic evolution, our long-term goal is to utilise this expertise and work with partners to develop tools and pipelines necessary for national/international surveillance, rapid detection/prediction of, and response to, disease threats to animals (wildlife, livestock and pets) and people (emerging zoonoses). Specifically, we plan to:

-Lead a programme of research into zoonotic influenza surveillance, risk and response (NIH CEIRR funding 2021-2028)

-Determine why children in communities adjacent to Lake Albert suffer high rates of schistosoma infections associated with peri-portal fibrosis despite good treatment compliance (EU funding, 2018-2022)

-[Text removed for publication].

b. *Food safety*

Food is a major route for disease transmission, with animal-derived products being responsible for most foodborne infections globally. Protecting public health through innovative, policy-relevant, multidisciplinary research that improves animal source foods' (ASFs) safety is this group's aim. RVC provides scientific evidence in support of actions to improve ASF safety preventing foodborne diseases. Javier Guitian leads this group. He has progressed from new lecturer (2002) to Veterinary Public Health Professor (2010). Working initially under Pfeiffer's guidance, he is now a leading veterinary public health researcher, co-ordinating multiple international collaborative projects. Food safety research builds on RVC's epidemiological strengths of risk assessment and probabilistic modelling pioneered by Pfeiffer and Guitian.

This expertise has been strengthened by the APHA partnership and joint OIE collaborating centre (see above). Guitian and Emma Snary (APHA; RVC honorary professor) lead these initiatives and hold mutual joint appointments (RVC/APHA), which together provide a large group of scientists and PhD students (100 in total). ASF safety is inextricably linked to food production systems and their socio-political contexts; RVC's strengthening of its capacity for Agri-health and Food Systems research (see below) has facilitated its food safety research impact.

RVC's research to improve ASF safety includes studies aimed at modernising meat inspection, pathogen-specific studies of major foodborne pathogens (e.g. Campylobacter) and theoretical research combining genomic and epidemiological metadata for future food safety surveillance. New appointees, **Ana Mateus** (from post-doc; 2014) and **Niko Dadios** (from Industry; 2019), have increased food safety research capacity. Recently awarded grants will address the most pressing food safety issues in LMICs (see below).

Our systematic meat inspection systems evaluation supports transition from conventional to risk-based approaches if data on the animals' origin suggests they pose no public health risk. Partly through RVC research, EFSA has endorsed this novel risk-based approach and a revised Europe-wide pig inspection system is being applied unless export requirements prevent this (Meat Inspection ICS). Working closely with the poultry industry, our research has motivated adoption of on-farm biosecurity measures that contribute to reduce human foodborne disease incidence (Campylobacter ICS).

Principal Achievements:

-developed a robust food chain model to combine 'big' data sources, including both genetic and high-fidelity epidemiological metadata

-modelled data from on-farm biosecurity measures quantifying their benefits in reducing campylobacter carcass contamination, informing industry practices changes

-Modelled risk pathways for hepatitis E virus pig carcass contamination showing that human health protection measures should focus on reducing entry of highly viraemic pigs into the food chain

Future plans:

As increasing volumes of higher resolution data become available, we will develop food safety surveillance systems that integrate epidemiological metadata and genetic data to protect public health. We will build on our proof-of-concept for data integration associated with machine learning for that purpose which was cited by the US National Academy of Sciences "Science Breakthroughs to Advance Food and Agricultural Research by 2030". Specifically, research on public health related to food safety in LMIC will:

-enhance chicken and beef safety, determining how poor people access these meats and how their safety can be improved to increase healthy nutrition in Peru (MRC; 2020-2022);

-devise ways of improving milk safety in Andhra Pradesh's increasingly intensified dairy industry (BMGF; 2018-2021);

-elucidate health and linear growth determinants in children with a focus on ASF and animal-related infections (UKRI Action Against Stunting Hub; 2019-2024).

c. *Sustainable Food Systems* *in changing social and political contexts*

Food safety cannot be guaranteed without understanding production systems. Thus, RVC research extends into Agri-health and Food Systems. Agricultural economics is a key discipline to integrate with knowledge of livestock systems in different cultures. Jonathan Rushton's appointment (2009) provided such expertise. Although Rushton moved to Liverpool (2016), Barbara Häsler had already developed food systems leadership potential. Her continued development has been supported by Bhavani Shankar (SOAS secondment, 2016-17) and Heffernan. Häsler now leads this area supported by new appointees **Pablo Alarcon** (from APHA, 2017) and **Mehroosh Tak** (from SOAS, 2019). Having three veterinarians (Häsler, Alarcon and Heffernan) with expertise in socioeconomic research puts RVC in a strong position to contribute to food security global challenges.

RVC brings these skills to both UKRI GCRF Hubs. The Action Against Stunting Hub uses transdisciplinary approaches to identify how local markets and value chains can deliver ASFs sustainably, safely alleviating infant stunting in Senegal, India and Indonesia. By combining quantitative and qualitative approaches from economics, nutrition, social sciences, epidemiology and microbiology, inefficiencies, threats and opportunities to improve safe delivery of nutritious foods are identified. In the One-Health Poultry Hub, chicken production and distribution networks in 4 Asian countries are being investigated to understand how to transform these systems to deliver food to rapidly growing human populations in a safe, healthy, equitable and efficient way.

Leverhulme Trust funding (2011-2016) established a network of LIDC-based Agri-Health researchers creating the Leverhulme Centre for Integrative Research in Agri-health (LCIRAH), an RVC, SOAS and LSHTM initiative. RVC contributes enthusiastically to LCIRAH activities, which funded both Häsler's and Tak's training. Centre funding continues through an LSHTM-led Our Planet Our Health Wellcome grant (2018-2022) 'Sustainable and Healthy Food Systems'. Using system dynamic models and group model-building techniques, Häsler is investigating key drivers of the chicken meat system (commercial and indigenous birds) in South Africa and their environmental, food security and safety impact. These models identify system-based solutions benefiting society.

This group has attracted MRC funding in collaboration with Liverpool University and ILRI. They have mapped livestock value-chains supplying Nairobi, using this to investigate the system's food safety risk practices and critical control points. Our growing reputation in food systems socioeconomic research is evident from increased funding attracted from quality sources. Debate about how much animal protein should be included in our diets, and the environmental and health impact of producing and consuming ASFs is multifaceted and polarised. To support these discussions, RVC investigates complex trade-offs between economic, environmental, and social

sustainability, including concerns about animal welfare, food safety, malnutrition and livelihoods, using transdisciplinary systems-based approaches applied to multiple projects (examples above).

Christine Nicol leads Animal Welfare contributions to this debate. Farm animals in Europe are increasingly group-housed where extreme physical restrictions (e.g. cages) are removed. Clear trends in this direction are apparent globally (USA, Canada, Australia and NZ). Animal welfare research has thus shifted focus from concern with effects of restriction to how animals can thrive in complex environments, and in their interactions with automated technologies. Good animal welfare will be facilitated by breeding and raising robust (adaptable to wide range of environments via innate regulatory pathways) and resilient farm animals (able to cope physically and emotionally with episodic challenges via learning and cognitive responses). To study this, we are collaborating with a global network of researchers to develop innovative measures of robustness and resilience, using novel automated technologies in poultry and cattle to record and validate movement, posture and behavioural structure as health and affective state indicators; investigating animal adaptation to automated technologies, (mobile monitoring robots); investigating early-life experience in generating robust and resilient phenotypes, including work on improving co-ordination, learning and navigation abilities of hens housed in >100,000 bird multi-tier systems, and nutritional and enrichment strategies to improve calf welfare. Humane slaughter of food producing animals is a major societal concern but a complex issue when incorporating cultural and religious beliefs. Gibson has sustained a research programme focusing on humane slaughter of poultry.

Principal Achievements:

-Completed laboratory-based comparison of performance and welfare of commercial fast- and slow-growing broiler chickens

-Contributed technical solutions to improve humane slaughter methods in a range of species

Future goals: Work on novel analyses generating holistic evidence, based on systems approaches, will continue to contribute to discourse on a new type of food systems governance, founded on One Health principles that supports policy changes. For example, we aim to:

-build a systems dynamic model of South Africa's transitioning, complex and dualistic ASF system with maximal stakeholder engagement, clearly identifying relevant problems and defining socially acceptable interventions (Wellcome; 2018-2022);

-develop a transdisciplinary food systems (TDFS) framework and methods for country-level analysis of changing food systems marred by long-term crisis (GCRF-AHRC: 2021-2023);

-develop methods and apply new technologies to predict and alleviate farm animal welfare problems.

d. *Host pathogen response and vaccinology*

Technical solutions to over-reliance on drugs in animal production require basic understanding of: (i) pathogens, (ii) host's immune responses to those pathogens **and** (iii) livestock systems. Knowing how these factors interact facilitates design of applicable technical solutions.

Damer Blake, leads this group which facilitates interactions between microbiologists, immunologists, geneticists, molecular biologists and bioinformaticians in a multi-disciplinary vaccinology team. Substantial capital investments supporting laboratory and animal-based research are underway (section 4) and new capacity-building and succession-planning appointments have been made. With particular focus on avian and porcine systems and intention to expand into aquatic species, the group aims to: (1) identify antigens that induce robust protective responses; (2) understand host-pathogen interactions at protein- and nucleic acid-level to identify optimal vaccine candidates; (3) develop flexible multi-species vaccine delivery platforms; (4) select farmed animal genotypes which respond most effectively to vaccination; (5) inform producer and consumer acceptance.

RVC has notable strength in developing vaccines for parasites. Apicomplexan parasites are highly represented, including Eimeria, Cystoisospora, Toxoplasma and Cryptosporidium (Tomley, Blake and Webster) and Theileria (Werling). New appointees: **Dong Xia** adds apicomplexan proteomic bioinformatics skills; **Ellen Knuepfer** (Crick Institute; 2020) brings gene-editing expertise applied to zoonotic *Plasmodium knowlesi* and *Babesia* spp. **Virginia Marugan-Hernandez** (from RVC post-doc; 2017) builds capacity in Eimeria vaccinology and **Androniki Psifidi** adds poultry genetics (host resilience) expertise, building on Larkin's fundamental avian chromosome evolution approaches; **Laura Buggiotti** (from CREA Agriculture Research Centre, Rome; 2016) adds further expertise in host genetics for resilience to infectious disease.

Genetics and candidate gene-led approaches have identified promising antigens. 'Omic' approaches are defining interactions between these antigens and host gene networks (Xia, Blake), with mapping and genome-wide association analyses optimising host responses and vaccine utility (Psifidi, Blake, Tomley). In response to demand from egg-layer industries, a series of 'omics' technology-driven projects aimed at poultry red mite vaccine development are underway.

For mass livestock dosing, flexible vaccine delivery technologies are key. Recombinant protein and DNA vaccine strategies have been supplemented with yeast expression systems suitable for mass oral delivery (Werling, Blake), as well as transgenic Eimeria parasites. Joint BBSRC/industry funding directly led to EU-H2020 funding to develop Eimeria as a novel vaccine vector, targeting veterinary and zoonotic pathogens. The ability to shuttle candidate antigens into various vector systems permits flexible responses to vaccine opportunities, directly targeting body systems and immune pathways.

Bacterial pathogens, particularly those infecting pig, cattle and dog respiratory tracts remain a significant interest. TRADIS (established through Rycroft's BBSRC LoLa), used to identify vaccine candidates, has been extended by Kendall to *M bovis* through BBSRC's Eradication of Bovine Tuberculosis initiative (LSHTM and APHA collaboration). Novel approaches to bacterial disease control beyond conventional antibiotics are discussed below (Antimicrobial Resistance Group).

This area is complemented through studies of evolution, epidemiology, behaviour and control of human and animal helminth and protozoan parasites (Webster) and modelling of anti-parasitic drug usage (Walker). Broader consequences of vaccination are also being assessed. Disruption caused by live Eimeria vaccination within enteric microbiomes has been defined, impacting on competitive exclusion and probiotic microorganisms (Blake). Recognition that successful vaccines must be acceptable to producers, legislators and the public is particularly important. Understanding vaccination cost-effectiveness (Alarcon, Häsler) and other socio-ethnical constraints on vaccine implementation strategy within different cultures is important for success (see SFS group).

Principal achievements:

-Produced annotated genome sequences of all seven Eimeria species infecting domestic chickens which will underpin new anticoccidial drugs and vaccines development and longevity

-Demonstrated importance of AMA in *E tenella* as a vaccine antigen candidate given the limited genetic and antigenic diversity observed and a conservative signature of selection

-Proved feasibility of oral yeast-based pig vaccination, representing a new cheap option for mass livestock vaccination

-Identified important mucosal antigen delivery pathways priming IgA and IgG responses

Future aims:

RVC's new Vaccinology Centre (section 3) will offer approaches from *in silico*, through *in vivo* trials, to field-based registration studies, supported by RVC Business professional staff. Strong connections with animal pharma will maximise opportunities to translated our REF2021 scientific achievements into products. Specifically we will:

-Use the One Poultry Hub platform and its flexible fund to work with industry developing yeast-based vaccines to improve poultry health and protect public health (UKRI-GCRF Hub; 2019-2024);

-Develop aquatic animal vaccinology through strategic collaborations with Stirling University;

-Identify new vaccine targets/antigens by combining glycomics and single-cell RNASeq, building on the C-lectin array success for cattle. By identification of targets recognised across species, develop carbohydrate-based vaccine platforms capable of combatting zoonotic diseases;

-Determine whether chickens can be selectively bred for increased resistance to enteric parasites and gut dysbiosis (UKRI-GCRF Hub; 2019-2024).

e. *Antimicrobial Resistance (AMR)*

This group provides an interdisciplinary approach to the global challenge of AMR. **Luca Guardabassi,** recruited (2018) to a joint appointment with Copenhagen University provides collaborative strategic leadership. A veterinary public health specialist with microbiological expertise, he is ideally qualified. He focuses on discovery of innovative antimicrobial drugs and diagnostic tests development optimising their use. This is highly complementary to pharmacologist, Pelligand, who co-leads the group. Guardabassi and Pelligand are members of EU VETCAST, an EUCAST standing subcommittee dealing with all aspects of animal bacterial pathogen susceptibility testing, including those with zoonotic potential.

RVC spinout, Tecrea Ltd., is developing novel technology identified by Liam Good which enhances antimicrobial entry into microbes, thus increasing existing drug efficacy and overcoming resistance. Tecrea Animal Health has been formed through a multi-million pound deal with a large Animal Health Company (see ICS). Pelligand is applying PK/PD principles and *in vitro* modelling techniques to determine optimal antimicrobial exposure profiles for problem pathogens and then translating this into optimal dosing regimens, through *in vivo* poultry studies. He is supported by Professor Toutain (Category C; honorary professor; 2017-2023). Good and Pelligand will work together on Alternatives to Veterinary Antimicrobial Drugs (AVANT), Guardabassi's EU-H2020 Innovation Action grant (2020-2024), which has a portfolio of non-antibiotic interventions targeting porcine diarrhoea. This builds on the polymer (nanoparticle) approach as an alternative for porcine enteric toxigenic *E. coli* treatment.

Two new appointments strengthen AMR research. Both are microbiologists with additional complementary skills developed during their post-doctoral training. **Lucy Brunton** (2017; from APHA), following post-graduate (RVC) veterinary epidemiology training, was appointed to strengthen AMR molecular epidemiology (focusing on extended spectrum beta-lactamase resistance). **Ben Swift** (2017; from Nottingham University), AMR strategic fellow, brings phage technology to bacterial diagnostics allowing AMR detection. These scientists add capacity to genome-based approaches to AMR epidemiology provided by Stuart Reid.

AMR research is important for Food Safety and Sustainable Food Systems groups. Understanding the drivers for antibiotic usage by farmers is crucial with on-going projects in India and Kenya (Heffernan; ESRC), in the UK Dairy sector (APHA collaboration) and with ILRI in the Vietnamese aquaculture system (CGIAR funding). We are using BBSRC DTP funding with associate partner, Food Standards Agency, to investigate AMR bacterial contamination of seafood (Mateus), identified as a significant risk because most seafood products are imported from countries with poor antimicrobial drug regulation.

Principal Achievements:

-Identified that polyhexamethylene biguanide's antibacterial action is through nanoparticle formation with DNA condensation and that it kills intracellular bacteria and protozoa without harming host cells

Future goals:

Continue to develop an environment that brings together people with diverse skills and perspectives needed to tackle AMR, broadening our perspectives to consider environmental contamination created by livestock use of antibiotics and nurturing the leadership potential of REF2021 new appointees. Specifically we will:

-model the comparative data on antimicrobial drug use, microbiome population dynamics and AMR gene prevalence to devise interventions that reduce AMR (UKRI-GCRF; 2019-2024);

-use a systems dynamic modelling to devise interventions to reduce antimicrobial usage in Vietnamese aquaculture (RVC/ILRI; 2019-2022);

-create a new AMR research platform to reduce livestock-sourced antimicrobial river contamination (GCRF Cluster programme – inception phase 2020-21).

2. People

Staffing strategy and staff development

REF5a presents high-level principles underpinning our staffing and development strategy, outlines key challenges we face around equality and diversity, attracting and developing clinician scientists for translational research and defines how we are tackling these. Here we define how our staff profile compares with REF2014 and reflect on turnover, retention and progression since 2008.

Our staffing strategy is supported by a Staff Development Manager with a research background dedicated to management and leadership development for early career researchers (ECRs), induction and training course design. RVC holds Athena SWAN Bronze (2018) and HR Excellence in Research (since 2012, last renewed in 2020) Awards. In 2020, we achieved the Association of University Administrators (AUA) Mark of Excellence award, recognising our commitment to professional service staff development. The behaviours framework underpinning this award has been adopted by academic departments and incorporated into new academic probation and promotion processes (APPP). This aligns perfectly with our commitment to the Research Integrity Concordat and membership of UK Reproducibility Network (UKRN).

RVC offers a strongly supportive environment, with a policy of seeking to develop high-quality people from the outset, and encouraging their ongoing development. Turnover of REF-eligible staff and progression of ECRs suggests our environment fulfils that policy, enabling researchers

to achieve their potential. Of the 113 staff returned in REF2014, 71 (62.8%) remain in post. Of those classified as ECRs (18), 11 remain employed, 10 having achieved promotion. Of the 7 that left, two clinicians moved into private practice and 3 have secured permanent positions in academic institutions (Harvard, Surrey and Liverpool John Moores) from RVC fixed-term independent posts. The other two moved to permanent academic posts at Hong-Kong City U and Imperial College after passing their RVC probation.

Seventy new appointments were made during REF2021, 35 of which are ECRs. Thus, we are investing in new talent but also appointing more experienced people to maintain this important balance. The rationale for many of the new appointments is presented above (section 1). Due to the change in REF criteria, the number of staff included in REF2021 has increased to 172 (52%). Of these, 31 people were in post in REF2014 but were not included. Twenty-three of these 31 are academics who provide clinical service and undertake research advancing clinical practice. Thus, REF2021 presents the breadth of our research. Equality diversity and inclusion data are shown in the Table below:

	Head count	M:F	Age (years)					Fixed-term contract	BAME
			29-35	36-45	46-55	56-65	≥66	(%)	(%)
All	172	1.0:1.0	14	66	54	35	3	11.0	12.2
New appts	70	1.0:1.8	14	37	14	4	1	24.3	5.7
ECRs	35	1.0:2.5	12	17	4	2	0	28.5	11.4
-REF2014	31	1.4:1.0	0	11	10	9	1	0	12.9
+REF2014	71	1.5:1.0	0	18	30	23	2	2.8	17.8

-REF2014 – staff in post but not included in REF2014; +REF2014 staff included in REF2014. Three of 172 people declared a disability (1.7%).

Our strategy for developing researchers entering their first academic post is to provide individualised career pathway (ICP) goals for their 3-year probation. Their work balance between teaching, research and clinical service determines the research achievements expected to progress. Support for research development is provided through internal funding to generate pilot data or set up external collaborations to learn techniques. Prioritised access to PhD studentship funding is provided (co-supervision with an experienced researcher is required). Current budget supports 28 students (£720k p.a.). Mentorship in grant writing is provided through research groups where resource sharing enables ECRs to get started. Residents are post-graduate students of clinical academics funded through clinical income.

We offer c.8 internally-funded PhD studentships per annum with stipends and fees for up to 3.5 years. Our goal is to provide new staff on research-focused contracts with a RVC-funded PhD student within 3 years with start-up funding for running costs. Applications are reviewed by RSC and projects deemed suitable are advertised; feedback is always given to help with grant writing. We advertise more studentships than we can fund to ensure we appoint the best candidates to their preferred project. Careful choice of co-supervisors ensures new staff are supported and integrate well. Independent Researchers can apply for PhD studentships on commencing their fellowships provided their posts last the duration of the studentship.

Since August 2013, 26 newly appointed staff (from REF2014 and REF2021) have been provided with PhD students from this source, showing we prioritise new appointees. Other priorities for Internal PhD funding is to provide students to staff recently awarded major grants, ensuring students enter supportive well-funded groups.

Of the 35 ECR included in REF2021, 8 were appointed into REF-eligible positions following a period of RVC post-doctoral training; 11 undertook either clinical specialist post-graduate training and/or their PhD at RVC prior to moving into REF-eligible posts. Four of these had both RVC clinical specialist and PhD training being part of our long-term strategy to develop clinician scientists (see REF5a). Three ECR clinician scientists are on internally-funded fellowships, collaborating with medical schools (Oxford and Kings) to develop major translational research programmes. All have secured Academy of Medical Sciences (AMS) starter grants. RVC persuaded AMS to accept veterinary applications. The strength of RVC's clinician scientist development programme is evidenced by appointment of RVC-trained clinician scientists to senior leadership roles elsewhere – 3 during REF2021, (Oliver Garden - Departmental Chair at University of Pennsylvania; Holger Volk – Departmental Chair, University of Veterinary Medicine Hannover; Karen Allenspach – Small Animal Medicine Professor, Iowa State University). Nevertheless, we recognise that we need to provide ICPs that play to individual strengths and for some specialist clinicians this will be clinical service combined with teaching. The clinician educator track (70% clinical service) is the role they fulfil. Academics on this track during their probation period do not take responsibility for research (see RVC's Code of Practice). This gives them time to establish themselves as clinical specialists and develop teaching skills. Once through probation we expect applied research contributions which advance clinical practice. The change to REF rules for REF2021 means these outputs are included.

The above data demonstrate we are creating opportunities for research assistants (RAs) and research-trained clinical specialists to progress, gain independence and access permanent positions. Progression to independence is facilitated by supporting RAs to be researcher co-

investigators on grants, recognising their contributions to proposals, providing access to small internal grants to generate new data or access training with collaborators to support their ideas and travel grants to attend meetings. Post-docs can be named as PhD supervisors when merited and access modular teacher training which they use to build a P.G.Cert Vet Ed. We support their applications for external fellowships, providing constructive feedback and committing to permanent posts at the end of fellowships where appropriate. Sixteen academics in our return have transitioned from independent research fellow (11 externally funded) into an open-ended position. Four more are on track to do so within the next 3 years. These are some of our most successful researchers, establishing their research within our environment before taking on academic duties. However, we recognise many post-docs will move into non-academic positions and our development and mentorship schemes equip them for this, as emphasised in our HR Excellence in Research Action plan (2018-2020). We have had excellent engagement with officers of the Researcher Association (RA) over the renewal process for this award (confirmed 12/2020).

We recognise that structured career development for established academics should be improved, through an institution-wide programme providing time and funding to develop new research skills. At present we support secondment and sabbatical proposals on an *ad hoc* basis when duties can be covered or income is generated to support replacements. The new ICP appraisal system provides transparent and more standardised routes for academic progression with options to tailor to the individual's circumstances (e.g. in terms of caring responsibilities) and strengths (use of optional goals) and is easily coupled to development requirements. Mentorship and coaching schemes support academic and non-academic staff. RSC has identified academic groups where leadership is required to facilitate mid-career researcher development and used secondments (Agricultural Economics), fixed-term part-time contracts (Animal Welfare) and honorary positions (Pharmacokinetics, Food Safety and Osteoarthritis) to provide (see Section 1).

Academics are encouraged to undertake consultancy/secondment work for stakeholders enabling them to experience different working environments. In some cases this is on an individual basis whereas sometimes academic groups work together to deliver what is needed. Our strong relationships with FAO, OIE, WHO, APHA, FSA and PHE make these frequent customers, assisting academic understanding of policy-makers' needs.

Academics are expected to engage in knowledge exchange, a mandatory ICP element, contributing equally with research, teaching and clinical service to probation and promotion. The close working partnerships we have with Industry and policy makers are highlighted in our impact case studies. Academic engagement with users of their research is also facilitated by HEIF funding (Concept Development Partnership Fund (CDPF)), supported by dedicated professional staff who help identify partners. This has been a major success in REF2021, assisting mid-career

researcher-development with GBP1,152,000 awarded since 2014-15 to fund 26 proof-of-concept projects ranging in size from GBP10,000 to GBP150,000, often with matched industry funding. In addition, RVC has received 2 separate BBSRC Impact Acceleration Awards (2017 and 2018), funding 4 projects designed to transfer know-how and skills to researchers in LMICs.

Research students:

We provide a stimulating training environment for PhD students, who are embedded within active groups. We aim to develop students as independent, innovative and critical thinkers, and future research leaders. The training environment is overseen by our Graduate School which delivers a strong and diverse transferable skills training programme, structured around Vitae's Researcher Development Framework. Skills development and research project progress are monitored through annual appraisal. Research students benefit from a wide range of support mechanisms, whether for academic matters or issues outside their immediate research environment. A mentoring scheme is provided for new starters who are also assigned an independent advisor. In 2019, we invested in Haplo™ PGR Manager, to bring all PGR student experience factors together in one user-friendly online system. Students record their development activities and progress in an easy-to-use online format. The appraisal process, thesis submission and examination procedures are embedded in Haplo™, which will replace current paper-based processes. Graduate School progression monitoring is much easier meaning struggling students can be recognised earlier.

We recognise the importance of partnering neighbouring institutions to broaden the experience and access to resources for our PGR students training to undertake research which goes across disciplines. Since 2007, RVC has been part of the Bloomsbury Studentship programme with Birkbeck, LSHTM, SOAS and UCL Institute of Education. During REF2021 the College has funded 14 studentships under this scheme, in which the students benefit from supervisors in two Colleges. RVC also provided co-supervision for studentships registered at partner Colleges.

Since 2012, RVC has been part of the BBSRC-funded UCL-led London Interdisciplinary Doctoral Programme (LIDo) with Birkbeck, LSHTM, King's College, QMUL, National Resources Institute, Greenwich and Royal Holloway, attracting c.10% of students in the programme which has run throughout REF2021 (grant renewed; 2020-2029). LIDo focuses strongly on applying quantitative methods to answer important biological questions and provides in-depth formal systems biology and bioinformatics training to support effective interdisciplinary research, thus aligning with RVC's strategic priority of training quantitative biologists (Section 1). LIDo's quality has been recognised through contribution of part-funded studentships by major stakeholders, including APHA and Food Standards Agency (FSA). RVC is ideally placed to provide training in global issues relating to food safety and security and zoonotic diseases in a One Health context. We have increasingly attracted key partners for joint studentships in these areas, including APHA at national level and the

International Livestock Research Institute (ILRI) internationally. We are one of the UK partners in the Africa-based SACIDS-PASET PhD programme, World Bank funded, providing student co-supervision and mentorship. Furthermore, RVC was the training lead in the ZELS PhD programme (2015-2019), hosting students conducting field studies in LMICs in collaboration with key stakeholders and policy makers. We are also a partner in 4 Marie Sklodowska-Curie Innovative Training networks (Bone Pain I&II, CarBon, and Tendon Train), all MSK Biology multi-institutional consortia involving industry partners.

In 2020, RVC became a partner in the GBP5,000,000 programme entitled 'Partnerships for Sustainable Food Future CDT', led by the Natural Resources Institute, Greenwich and involving five other HEIs and two research institutes. The UK's only Food Systems CDT, awarded competitively by BBSRC, its goal is to drive transformation of the UK food system, and ensure safe, healthy, sustainable, and affordable food for all. Barbara Häsler played a leading role in designing the CDT's training programme.

RVC has sustained its success in attracting industry partners for PhD training. Of 188 PhD studentships registered since August 2013 (average of 27 per annum), 47 involved industrial partners (25%); 41 (22%) were UKRI funded. We have awarded 181 (1.05/fte submitted staff) PhD degrees since August 2013, 81.5% of which were awarded within 5 years of registration (<7 years if part-time) with 16/34 late completions having interruptions for maternity and/or medical reasons. Considering clinical academics train post-graduate clinical specialists (38% of RVC staff are practising clinical specialists) in their disciplines (including research training) with 129 graduating (MVetMed) over REF2021, 1.80 PG students trained/fte is a more appropriate metric.

Equality and Diversity

The challenges we face, relating to gender equality, are significant and our institutional-level approach to encouraging women to take up leadership positions and to the issues raised by the Black Lives Matter campaign are outlined in REF5a. Since 2014, RVC has taken significant steps to ensure our environment caters for a diverse researcher population and treats them fairly. A dedicated HR Equality and Diversity Manager has been appointed and each department has Equality and Diversity Champions. The Equality and Diversity Committee (EDC) chair sits on the senior decision making committee, determining College policy and resource management. RVC achieved the Athena Swan Bronze Award in 2018 and is working towards the Silver award. We work hard to ensure staff are trained to minimise unconscious bias during recruitment, requiring all appointment board members to have undergone this training (refreshed triennially). Our new APPP process has improved transparency and objectivity in decision making. A professorial grading system has been introduced (2020). Professors were moved onto a new salary scale, the final modernising step to our APPP process. All academics are provided with ICPs with mandatory

elements and are required to comply with our Behaviours Framework designed to foster a supportive and inclusive culture. In 2018, flexible working was promoted through workshops, resulting in increased Policy awareness and a 54% increase in flexible working requests (31 in 2017-18 vs. 48 in 2018-19).

Contract researchers are represented on our EDC and RSC and in the 2020 internal Researcher Association survey, 87% of 45 respondents felt RVC is a fair, caring and inclusive place to work. Nevertheless, we endeavour to continually improve the research culture, accepting that we need to build on the 2020 AUA Mark of Excellence Award and develop an active bystander culture, implement a 'report and support' system reinforcing the behaviours framework and ensuring inappropriate behaviours are called out whenever encountered.

3. Income, infrastructure and facilities

Average research income per annum during REF2021 has grown by 23.3% relative to REF2014. REF5a explains the strategy to maintain a balanced funding portfolio. EU-Government funding has increased 2.6 fold because of a deliberate strategy of educating academics in the EU-funding landscape, building on the success of using consultancy to assist in bid preparation. These approaches have led to 25 awards running over the REF2021 period, including four ERC Investigators, five individual Marie Sklodowska-Curie fellowships and four ITNs. RVC academics were/are partners in 9 EU-consortium grants (3 are EDCTP programmes). We have invested in professional staff capable of supporting consortium-building activities and identifying additional large collaborative funding opportunities (see REF5a).

ERC funding has enabled Alan Wilson to publish high quality innovative research culminating in his election to FRS (2020). His work is of major public interest, has featured on BBC Horizon (Cat Watch 2014: The Horizon Experiment), where technology developed for measuring performance of wild cheetah was applied to domestic cats in suburbia; a public interest cat behaviour experiment. Technology developed in his ERC award is being enhanced through two ERC Proof-of-Concept grants to ensure it has broader impact and application.

The same outgoing collaborative approach leading to success in accessing EU funding has brought success in leading consortia involving LMICs in response to UKRI-GCRF Initiatives. GBP3,000,000 awarded to RVC has provided resources to overseas partners during REF2021 (excluded from research income data). Support for interdisciplinary team development through LIDC is described in section 1. Many IRLFS researchers are highly motivated to positively impact the lives of the world's poorest people. The UKRI Hub grants secured provide unrivalled platforms on which to build. Management of such large scale international projects is challenging. RVC has invested in project management support staff and now employs 3.2 fte whose salaries are

recouped from grants where possible. We have also invested in a Research Information Management System, Worktribe™, providing sophisticated research management tools.

To maximise impact from our GCRF activities, RVC leads a Connecting Capability Fund project (Research England), The Bloomsbury SET. This £5.6-million project, led by RVC's Director of Research Administration (a new Professional Service appointment for REF2021), involves RVC, LSHTM, SOAS and London School of Economics. It focuses on development of diagnostics, vaccines and artificial intelligence applications to infectious disease modelling (stemming from IRLFS research; section 1). It supports three 2-year Innovation Fellowships for ECRs (2 at RVC, 1 at LSHTM), and nine 2-year project grants with industry/user involvement through co-funding and joint supervision.

The Bloomsbury SET's Advisory Council is drawn from industry (mainly SMEs), government bodies (e.g. PHE) and NGOs. This provides advice and guidance to the Steering Committee, conducts peer review, and facilitates new connections with industry, state actors and public-private partnerships, such as transnational Product Development Partnerships that are developing new diagnostic tools and vaccines. Success in securing Research England follow-on-funding for Bloomsbury SET (GBP4,000,000; 2021-2023) creates a remarkable opportunity to collaborate with the Infection Innovation Consortium (iiCON) from North West England and operate an ambitious 'Impact Connector' model enabling tailored commercial support for our strongest projects through the core Accelerator element, increasing the pace at which they move towards TRL 7-9. The Poultry Hub is also stimulating engagement with UK and European industry (e.g. vaccine manufacturers), and with poultry producers in LMICs in South and South-East Asia.

A major future goal of our pathogen-based research is to reduce reliance on chemotherapy by developing endemic pathogen vaccines. Hence, we are creating a Veterinary Vaccinology and Cell Therapy Hub (VCTH) in partnership with Herts LEP (see REF5a). This opens in July 2021. In addition to modern laboratory and office space, it includes SME space adjacent to academics enabling shared access to equipment. The facility is equipped with state-of-the-art cell sorting and analysing machines (GBP471,254), and fluorescent microscopy (GBP83,501) run by experienced newly appointed managers. This facility complements our Camden microscopy unit where the confocal microscope was renewed in 2019 (GBP250,026) through our rolling replacement programme. Sharing of equipment is a two-way process and the Merck group in LBIC allow RVC mitochondrial biologists access to their Seahorse equipment for cellular energetics analyses.

Livestock vaccine development requires pathogen challenge studies and we have invested in our custom-built barn, equipping five rooms with individual air-handling systems and HEPA filtration. This enables work to SAPO 3 level, including exotic disease causing organisms such as

Theileria and *Babesia spp*. Large animal experimental facilities for regulated work are used extensively by external partners alongside RVC academics. For example, we maintain animals providing reagents for the National Institute for Biological Standards and Control, breed genetically modified pigs for heart valve-replacement research (UCL-led programme) and work collaboratively with UCL and Sheffield University in our GLP-registered facilities, developing human orthopaedic implants.

Our Biological Services Units (BSU) on both campuses have been completely refurbished and plant replaced (2016-19; GBP3,712,397). This accommodated expansion of dog breeding facilities for our DMD model, successfully characterised with Wellcome Bioresources funding (see section 1), a resource now available for collaborative working. Industry are funding trials to develop data for registration studies, hence the need to expand the facilities. A 3Rs project is underway to sort semen so only male puppies are produced, reducing the numbers of dogs that need to be bred. BSU staff are dedicated to rehoming dogs wherever possible.

Further investments in experimental facilities for translational research include installation of a fluoroscopy unit (GBP143,500) enabling cardiac catheterisation. [Text removed for publication]. We plan to expand our large animal translational model programme to complement our basic science and clinical expertise in cardiovascular biology and neurosciences through creation of an advanced imaging centre (3T MRI) run by clinical specialists. Co-funded by the Herts LEP (GBP2,127,000) this opens in Jan 2022. We envisage cell therapy and gene editing will be utilised extensively in these models, leading to treatments for chronic degenerative conditions in human and veterinary patients. Thus, we have established a Stem Cell Centre (SCC), licensed by the Veterinary Medicine Directorate, producing cells for veterinary use. HEIF funding is pump-priming SCC's staffing, which will become part of the LEP-funded VCTH. We are actively pursuing partnerships with companies associated with the Stevenage Cell and Gene Therapy Catapult Manufacturing Centre.

As part of our strategy to use veterinary patients as human disease models, we have invested in state-of-the-art facilities for single cell sequencing from clinical material (10xGenomics machine; USD128,125). Dedicated technicians trained by the WCHG, Oxford manage this facility. Parallel investments in high-performance computing (GBP199,643) have upgraded our cluster, and new bioinformatics appointments (Section 1) support this. We have maintained a group of veterinary nurses to support clinical sample acquisition, charged to research grants but employed on permanent contracts through the Clinical Investigation Centre. These staff archive clinical samples where owner informed consent is provided. IT investment in hospital and laboratory information management systems (ongoing) and VetCompass™ completes the tools we provide for clinical research. A dedicated IT developer manages these systems. We have invested in IT staff training to develop their natural language processing skills, facilitating text mining capabilities, which will

also benefit our social science research. Finally, as a commitment to advancing primary care practice, we have purchased a primary care practice in Bedford. This centre will facilitate primary care-based clinical research, complementing partnerships we have with the PDSA and Blue Cross and Beaumont Sainsbury Animal Hospital in so doing.

4. Collaboration and contribution to the research base, economy and society

We generate new knowledge through excellent basic biological, biomedical, veterinary applied and clinical research in order to advance science, and enhance human and animal health and welfare. The Institutional-level strategies to facilitate effective knowledge exchange are outlined in REF5a. Our 'One Health' approach to research means its beneficiaries encompass a broad range of stakeholders. Working in partnership with these groups is important to understand the context in which the knowledge generated is used to provide solutions to their problems.

Evidence of RVC's broad international reach can be gleaned from the Veterinary Science QS University World Rankings. RVC has been in the top three institutions globally since Veterinary Science's inclusion (2016), ranking 1st in 2019 and 2021. Academic reputation, weighted for international views, comprises 40% of the ranking score.

Fostering academic interactions

Often academic partnerships are best established 'bottom up' with collaborations being established through shared interests. To foster interdisciplinary research, RVC as a stand-alone veterinary-focused institution needs to form lasting partnerships as a framework for collaborations. Staff in the Research Support Office (RSO) actively identify opportunities to apply for large consortium grants and work with lead academics identifying appropriate partners. LIDC is a major enduring partnership established in 2007, providing access to many disciplines needed to tackle global challenges outlined in section 1. Within LIDC, LSHTM's interests align most closely with RVC's and many academic partnerships have grown following initial introductions at LIDC or via PhD co-supervision through the Bloomsbury Research Studentship scheme. The VPR-I sits on LIDC's Management Committee, line manages its Director and chaired the Bloomsbury Research Committee (2012-2016).

The LIDo DTP is a second institutional-level academic partnership facilitating interdisciplinary working between biological, physical and mathematical sciences. The academic partners are detailed in section 2. RVC is a LIDo founding member and has provided leadership of its Management, Research and Training and Partnerships Committees during REF2021. LIDo encourages cross-institutional co-supervision from different disciplines which applies to 46% of our standard LIDo studentships. It enables us to build on existing collaborations with scientists working at 3 of London's largest medical schools (important for our One Health Strategy). Our RSO has co-ordinated show-and-tell symposia at UCL (Biosciences Division and Dept. Medical

Physics and Biomedical Engineering) and QMUL (focusing on MSK Biology, Cardiovascular Biology and Comparative Genetics). Collaborations with Kings are strong in Neurosciences and Cardiovascular Biology. RVC and Kings jointly fund a Clinician Scientist Fellow in Neurosciences. The new LIDo partner, NRI (Greenwich University) provides complementary expertise for Food Systems research. NRI led the successful application for the UK's Food System CDT in which RVC is one of seven partners (see above).

In preparing for submission of the UKRI-GCRF One Poultry Hub bid, our wider shared interests with the Zoology Department, Oxford University became apparent. This resulted in a joint appointment (in Genomic Epidemiology – section 1) and a MoU (2018-2023) setting out the ways in which we intend to collaborate. In 2019, two symposia were held to explore areas of collaboration, including sharing of resources, and joint grant applications resulted. The Covid-19 outbreak has curtailed face-to-face interactions necessary to progress this relationship to its full potential. Support for our comparative genetics strategy is particularly important and strong relationships have been forged with WCHG, Department of Medicine in Oxford through Davison, who holds a visiting position there, mentoring veterinarians who have enrolled on the Wellcome-funded 4-year clinical PhD programme to which RVC is affiliated. In the field of antimicrobial resistance, academic collaboration with Copenhagen University has resulted in RVC's involvement in a H2020 Innovation Grant and a senior joint appointment to provide RVC leadership in AMR (section 1).

Institutional-level partnerships have also been fostered with UK-based Research Institutes, where RVC's strength in particular academic disciplines is sought after. We have strength in depth in pathology, employing specialists with laboratory animal pathology expertise and work collaboratively with the Francis Crick Institute to ensure their scientists use the most appropriate models, design experiments correctly and interpret molecular pathology changes accurately. This partnership provides excellent development opportunities for our ECR pathologists who alert Crick scientists to relevant veterinary patient models. We provide The Pirbright Institute (TPI) with expertise in Veterinary Epidemiology, under a MoU (2019-2022) supporting them in developing their ECR epidemiologists. This builds on longstanding TPI collaborations on chicken viral diseases (Professor Munir Iqbal holds an honorary RVC position) and PPR, where multiple joint grants have resulted through complementary expertise.

To ensure we work with academic partners to maximise our research impact, RVC leads a Research England-funded CCF project, The Bloomsbury SET (see section 3). In addition, we are a partner in the MedTech Super-Connector CCF led by Imperial College.

Non-academic users of our research include:

(a) **Industry** (Biomedical and Animal Health [encompassing Pharmaceuticals, Diagnostics, Medical Devices]; Agriculture and Horticulture Development Board, Animal Nutrition, Biotechnology and robotics businesses)

(b) Government **policy makers**, veterinary drug registration agencies, non-governmental organisations, e.g. FAO, OIE and WHO, and charities involved in public health and infectious disease control

(c) All areas of **professional veterinary practice** – companion, production animal and equine practice at first opinion and referral levels, wildlife medicine, government service for public health and food safety and security. Additionally, through translation to human medicine, human health care provision systems

(d) **Communities and individuals** - particularly those affected by disease or injury, including organised patient groups; pet owners; and those concerned with animal welfare or food safety e.g. farmers and animal charities, together with all affected by socio-economic consequences of zoonoses

(e) **Public** (adults and school-age children) and **media** – engagement has been directed towards fostering greater understanding of and enthusiasm for our science and natural history

High level strategies for fostering interactions with each of these groups are detailed REF5a. Further details follow.

Industry

Strong engagement with industry is evident from the proportion (20.2% in REF2021) of our research funding from collaborative R&D contracts with private organisations world-wide. In addition, 25% of PhD students registered over REF2021 worked on projects with industry partners. Furthermore, 10.7% of our original research publications include corporate co-authors (Scopus), demonstrating that the research is often an intellectual partnership.

We support industry engagement through: a) matched funding initiatives supporting collaborative R&D (proof-of-concept); b) provision of space for 30+ Life Science businesses at LBIC, RVC's central London innovation hub; c) proactive marketing of College expertise, services and facilities; d) industry showcase events; e) researcher support and training in technology transfer, including the licensing of College-owned intellectual property; and f) policy engagement with corporates and small businesses in London's Knowledge Quarter (KQ) and Hertfordshire, aiming to contribute to Local Industrial Strategy delivery.

Academic consultancy is encouraged with up to one day per week of consultancy permitted to boost personal income or discretionary accounts. The RSO helps academics to find industry partners for iCASE studentships and grant applications requiring industrial partners (section 2).

We have engaged two Entrepreneurs in Residence to work with researchers in understanding the routes to commercial impact of their work.

RVC established the first London-based innovation centre for commercial companies in 2000 (LBIC; section 3). Demand for LBIC space is very strong, extending to larger companies as well as SMEs. The LBIC CEO (who also leads RVC Business) and VPR-I work together to ensure companies whose interests align with RVC's research strategy are recruited. Preference is also given to companies interested in accessing/sharing RVC resources (equipment, animal facilities). Such sharing increases contact with RVC staff and contributes to running costs. RVC Business will operate the new SME space (VCTH) from July 2021. As a member of One Nucleus, RVC hosts a 'Bio-Wednesday' networking event annually. We actively promote One Nucleus's events to academics.

Four of our impact cases studies demonstrate our success of achieving impact through working with animal health industries. Further examples of on-going work that is at an earlier stage and will likely generate future impact follow. Our strategic approach to engaging with medical pharma and device companies was explained in preceding sections. Our large animal experimental facilities are registered with MHRA for GLP studies [text removed for publication]. Similarly, novel treatments for DMD are being developed collaboratively in proof-of-concept trials using our dog model prior to human clinical trials. SML research informs bioinspired robotics. Those interested in flight have studied how insects sense proximity of objects and the ground whilst in flight [text removed for publication]. Further work on how birds adapt to turbulent airflow is being used to inform aircraft wing design and has led to a patent application. Collaboration with the Government's DSTL in further R&D in a third concept derived from insect flight, echolocation, is ongoing. Finally, RVC researchers whose work with FSA informed the on-farm biosecurity measures to reduce broiler carcass contamination with Campylobacter, have worked collaboratively with Aviagen to develop a simulation model to assess the effectiveness of measures designed to reduce the risk of introduction and contain spread of infection between poultry facilities.

Policy-makers:

RVC encourages participation in regional, national and international bodies making and influencing policy, as well as in schemes to develop political awareness. The institutional-level relationships with APHA, OIE, FAO and WHO are detailed in REF5a and elsewhere in REF5b. RVC has consolidated its position as a trusted provider of consultancy and services to national and international bodies including the European Commission; FAO, WHO and DEFRA. Twenty-three RVC academics have served on national, European or International committees providing scientific advice to inform policy. RVC is recognised by the European Food Safety Authority

(registered provider) and a preferred provider for DEFRA. Strong links with private consultancy organisations provide complementary expertise when required to address specific project proposals. RVC is a partner of ILRI, the CGIAR-funded global research partnership for a food-secure future.

Four of the submitted ICS demonstrate how our research is used to inform policy in the UK and internationally. Other examples include work informing policy to control highly pathogenic avian influenza in the socioeconomic context of Bangladesh's poultry industry where trade in live poultry is an important income source for small-scale farmers. RVC's ZELS-funded programme, Behavioural Adaptations in Live Poultry Trading and Farming Systems and Zoonoses Control (BALZAC) has recommended that policy should be based on the One Health concept and that the policy environment should be modified to enable formal multi-sector engagement, clear roles and responsibilities, a common pool of transferable resources, and the creation of an inter-ministerial One Health secretariat to facilitate this process. With this platform in place, detailed research insights have contributed to new policy development aiming to improve Bangladesh's avian influenza control. Continued research in collaboration with TPI into African Swine Fever virus has provided new information on virus transmission dynamics, demonstrated how the infection can spread without being detected in low-biosecurity pig farming systems, thus emphasising the challenge and critical importance of surveillance for early detection. These insights have informed OIE and FAO policy recommendations for control of this transboundary disease, recommendations which are being adopted by the European Commission. Brucellosis research in Jordan, West Africa and India has established the extent of the public health problem and epidemiological risk factors, is informing local context specific control strategies (in India implementation impacted by the pandemic) and establishing diagnostic laboratory-based skills capacity to detect infection (West Africa).

Professional Veterinary Practice

RVC has a tradition of providing leadership within the veterinary profession. In REF2021, RVC academics have led RCVS (two presidents) and BVA. Engagement with first opinion and specialist practitioners ensures research focuses on common important clinical issues and provides access to data and case material for research. Relationships with charities (e.g. PDSA, Blue Cross, Battersea Dogs and Cats Home, Redwings Horse Sanctuary) facilitate substantial projects with unique longitudinal data collection. Examples of these feature in our ICSs. VetCompass™, RVC's system to enable veterinary practices to share data for research purposes, has tripled in size since REF2014, with 1800 practices and 15,000,000 animals providing data, including Equine Practices since 2016. Research using this system and has helped industry, welfare charities and government understand what diseases are seen in veterinary practice and how they are treated. Plans for further VetCompass™ development are included in section 1.

RVC research is also translated through conventional dissemination routes: its own Continuing Professional Development (CPD) programme; textbooks; and national and international conference presentations. During REF2021, RVC academics have co-authored 23 articles providing best practice consensus guidelines through International specialist colleges and special interest groups, evidence our clinical scientists are innovating in their fields. Three ICS describe RVC research that has changed clinical practice (reflected in consensus statements). Other examples where RVC research is influencing veterinary practice include: (i) equine laminitis research where refinement dynamic oral sugar tests and validation of plasma adiponectin assay allow accurate identification of high risk animal and so targeting of preventive measures; (ii) growth hormone-producing tumours, diagnosed by measuring serum IGF-1 (assays offered commercially), has been identified as a treatable cause of feline diabetes mellitus. RVC research has informed a number treatment options for this newly recognised form of feline diabetes.

Community and Public Engagement:

RVC's Widening Participation and Community Engagement team works closely with researchers to enthuse schools; groups recognised as hard-to-reach for higher education; and other community groups in RVC's research. In REF2021 period, over 107,000 participants have attended events where RVC researchers have inspired young people and community groups with new discoveries and innovations. A highlight was our involvement in the BBSRC Great British Bioscience Festival in November 2014, Bethnal Green (Structure and Motion lab research). A series of 13 research-themed 'RVC Late' public open evenings have been held throughout REF2021 attracting 7223 bookings to attend. These events allow the public to talk to scientists leading to discussion about animal use in research, which is part of RVC's commitment to the Openness Concordat (see above). Researchers involved in work to identify treatments for rare diseases affecting children (e.g. DMD, Batten's disease) engage directly with patient groups.

Media Interactions:

RVC invests significantly in promoting its research outputs and impacts through the media. A centrally-managed professional team supported by specialist consultants collaborate with our researchers to promote our research and deliver bespoke campaigns for particular projects.

During REF2021 we issued 516 research-specific press releases generating 22,741 press stories which compares favourably with international competitors. Content has been covered by 1,388 different publications and broadcast media in 69 countries. RVC content has featured on UK terrestrial television both nationally and regionally as well in countries such as USA and Ireland.

Research news releases posted on our website have been read 69,823 times by 60,685 individuals. Our main social media channels have 136,738 followers. Our social media posts (1,874 in this period) have been seen by 19,100,000 people with RVC specific research stories being featured 850 times since 2016.

This extensive social media and general media coverage has increased awareness and participation in our research surveys. Our DMD canine model featured on ITV News at Ten in 2018 after its publication in 'Science', winning an UAR Openness Award in 2018. This contributed to RVC being granted UAR Leader in Openness status (2019-2022).

Broader contributions to the subject area

RVC academic staff actively contribute to the broader subject area through serving on grant awarding committees (37 members of international and 44 members of national committees) including 3 committee chairs. Academic staff hold 129 journal editorial board memberships, with 26 as editor-in-chief and reviewed over 4560 journal articles and 1500 grants applications during REF2021. In addition, RVC staff have organised >180 conferences and have delivered >400 Plenary or Keynote conference lectures and >1200 invited oral presentations. RVC hosted 214 visiting researchers, provided supervisory input to 148 PGR students registered at other institutes. Within our new appraisal system (section 2), these and other knowledge exchange activities where audiences are non-academic, are an expectation. Opportunities to apply for national and international committees are circulated by the VPR-I and RSO colleagues encouraging individuals to apply. Recognition of RVC contributions to the subject area has resulted in 140 prizes/awards being received during REF2021 period.

Knowledge exchange strategy and future goals

To maximise the impact of its research, RVC's Knowledge Exchange Strategy 2016-20 supports the undertaking of knowledge exchange activities internationally, mainly in least-developed or LIMCs. This involves partnership development for training and capacity-building, with the aim of tackling neglected zoonotic diseases influencing human and animal health; to understand factors that influence pathogen flow from wildlife into domestic animals and people; to determine factors associated with intensification of livestock production that drive unintended consequences (e.g. antimicrobial resistance, emergence of zoonotic diseases); and to develop field diagnostic tests and platforms for vaccine delivery. These areas contribute to the Government's aim of addressing the United Nations' Sustainable Development Goals 1 to 3 (elimination of poverty and hunger; better food security, improved nutrition and sustainable agriculture; healthy lives).

During REF2021, RVC has substantially increased its efforts to help deliver the People and Place elements of the UK Industrial Strategy. This engagement has enabled the small team in RVC's

RSO to shape local industrial strategies, and thereafter respond to the economic development and regeneration needs identified therein (e.g. working with Stevenage Bioscience Catalyst to secure a Life Sciences Opportunity Zone in Hertfordshire; collaborating with KQ London Ltd. to champion a new central London innovation district). RVC's approach has been to lead these responses where opportunities have presented themselves – for example, the BEIS Science and Innovation Audit of the KQ (2018), The Bloomsbury SET (2018-21, funding from Research England's CCF) and funding for science infrastructures (2018-24, Local Growth Fund for Herts – of which RVC is the single largest recipient).

In response to the Knowledge Exchange Concordat, RVC is benchmarking its performance against other STEM specialist institutions, to create an action plan that facilitates continuous improvement through investment in people and infrastructures.