Veterinary Biologics and Biosimilars: *Routes to Approval and Commercialisation in the U.S., EU, and UK*

Biological veterinary medicinal products ("biologics") are an innovative and fast-growing component of the veterinary pharmaceutical market. Biologics provide veterinarians with valuable new treatments to improve the health and welfare of their animal patients by addressing unmet need, while providing value to pet owners. Biologics differ from traditional pharmaceuticals because they are produced by, or extracted from, a biological source and therefore may have different regulatory considerations. Of note, in the U.S., animal biologics are subject to the regulatory oversight of the U.S. Department of Agriculture (USDA) rather than the U.S. Food and Drug Administration (FDA), which regulates other therapeutic products, including animal drugs. In contrast, in the UK and EU, biologics do not have separate regulatory frameworks or regulators and there are clear approval routes for biosimilars. In this article, we provide a practical overview of the regulatory considerations for approval and commercialisation of biosimilars in the U.S., EU, and UK

Routes to Market Authorisation in the U.S.

In the United States, animal biologics and animal drugs are distinct categories. The definition of animal drug is very broad, under the Federal Food, Drug, and Cosmetic Act (FDCA) and includes any substance "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals," 21 U.S.C. § 321(g)(1) In contrast, animal biologic is a much narrower category – in addition to a general intended use requirement "for treatment of animals," an animal biologic must fit certain subject matter and mechanism of action criteria. If a therapeutic product does not meet both of these additional criteria, it is not regulated as an animal biologic and generally, by default, will be considered an animal drug.

Both product categories require premarket authorization – licensure for biologics, and approval for drugs – but they are regulated under different statutory frameworks implemented by different agencies, and are thus subjected to different regulations.

Animal Biologics

U.S. animal biologics are regulated under the Vaccine-Serum-Toxin Act[1] (VSTA) by the Center for Veterinary Biologics (CVB) in the USDA Animal Plant Health and Inspection Service (APHIS) Veterinary Services. This distinct jurisdiction grew out of early 20th Century concerns about tainted vaccines for livestock, a category not then regulated by the precursor to the FDA, and has remained with USDA ever since. The regulatory requirements for licensure of an animal biologic by CVB are generally determined between CVB and the sponsor, in a manner distinct from the FDA approval pathway for animal drugs.

Under USDA regulations, an animal biologic includes "all viruses, serums toxins (excluding substances that are selectively toxic to microorganisms), or analogous products" at any stage of production, shipment, distribution, or sale, for use in the treatment of animals. In addition to this subject matter requirement, the definition also requires that the substance "act primarily through the direct stimulation, supplementation, enhancement, or modulation of the immune system or immune response."[2] The regulations include examples of the types of products that may be included in this definition, among them vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, immunostimulants, certain cytokines, antigenic or immunizing components of live organisms, and diagnostic components, that are of natural or synthetic origin, or that are derived from synthesizing or altering various substances or components of substances such as microorganisms, genes or genetic sequences, carbohydrates, proteins, antigens, allergens, or antibodies.[3]

Elsewhere, APHIS explained what it means for a product to act primarily through the direct stimulation, supplementation, enhancement, or modulation of the immune system. Specifically, it stated that "stimulation" refers to active immunization, "supplementation" refers to passive immunization (such as through blood or other components), and "enhancement" or "modulation" refers to the upregulation or fine-tuning, respectively, of the immune system to generate an effective immune response.[4]

The VSTA authorizes USDA to ensure that veterinary biologics are pure, safe, potent, and efficacious.[5] Today, licensure for a new animal biologic by USDA requires preclinical and clinical studies demonstrating purity, safety, potency, and efficacy in target species,[6] facility and product licenses, including facility inspections, and labelling review to ensure claims are supported[7] by product data and license conditions.[8] USDA has also issued guidance that describes a case-by-case basis by which it determines the scope of regulatory requirements. Notably, under the VSTA, there are no user fees for animal biologics licensure, no fixed timeline for review, and no pathway for approval of animal biosimilars. In addition, and in contrast to the animal drug pathway, there are no available regulatory exclusivities.

Animal Drugs

Animal drugs, on the other hand, are regulated under the FDCA by the FDA Center for Veterinary Medicine (CVM). Importantly, products intended for the treatment of animals that do not fall within the scope of the animal biologic definition are, by default, regulated as animal drugs, which has a much broader definition.[9]

The definition of drug in the FDCA includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals."[10] Notably, FDA will regulate articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of animal disease "if the primary mechanism of action is not immunological or is undefined (unknown)."[11] Approval of an animal drug requires a showing that the product is (1) safe for the animal, (2) safe for humans consuming food from treated animals, and (3) effective for the intended use. 21 U.S.C. § 360b(d)(1). When a new animal drug application is submitted to FDA's Center for Veterinary Medicine (CVM) for approval, CVM evaluates the drug for safety and effectiveness, and as part of the review process, determines whether the drug will be classified as a

prescription only drug, a veterinary feed direction (VFD) drug for use in animal feed, or as appropriate, an over-the-counter (OTC) drug.

US Summary
The distinct statutory authorities for USDA and FDA make determining whether a product is an animal biologic or drug central to the discussion of regulatory approval. As novel biotechnologies develop, the definition of a biologic and three-step inquiry will determine under which authority new products will be approved. Whether an animal therapeutic is classified as a biologic or a drug will have significant implications for regulatory approval and oversight.

Routes to Approval in the EU
Biologics, like other veterinary medicinal products, may only be placed on the EU market with a valid marketing authorisation (MA). An MA is comprised of a decision granting the MA issued by the relevant competent authority, and a technical dossier with the data submitted by the applicant in accordance with the EU Veterinary Medicines Regulations (EU VMR). Specific requirements for biologics are provided in Section III of Annex II EU VMR, including potential flexibilities to Good Manufacturing Practice (GMP) requirements. In the EU, biologics are typically authorised through the mandatory centralised procedure, resulting in an MA valid across all EU 27 and EEA 3 States. Under the centralised procedure, the MA application is submitted to European Medicines Agency (EMA). The scientific evaluation is carried out by the Committee for Veterinary Medicinal Products (CVMP) of the EMA.

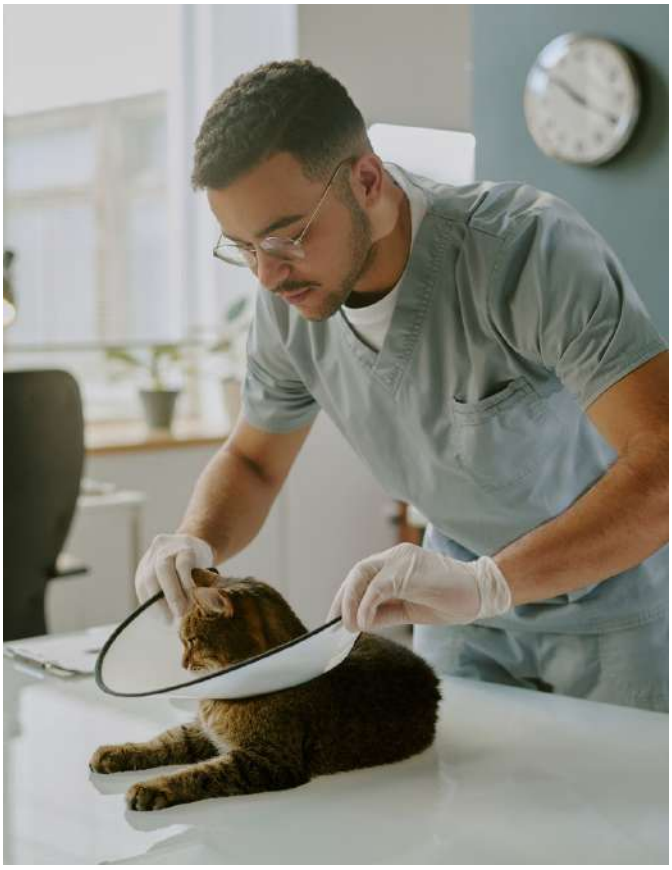
CVMP will assess the "benefit-risk balance" by evaluating the positive effects of the biologic in relation to any risk relating to the quality, safety, and efficacy of the VMP as regards animal or human health, any risk of undesirable effects on the environment, and any risk relating to the development of resistance. The EU Commission determines whether or not to grant the MA after consulting the Standing CVMP (which is composed of the representatives of the Member States and chaired by the Commission).

In the future, EU veterinary biotech products could also benefit from additional valuable IP protection which may help incentivise their development. Specifically, under the recently proposed EU Biotech Act (which still needs to go through the full legislative procedure), veterinary medicinal products developed by means of biotechnology processes to diagnose, treat or prevent zoonotic diseases (diseases transmissible between animals and humans) may be entitled to an extension of their supplementary protection certificate (SPC), which would effectively extend their patent protection for the product by one year.

Manufacturing and Supply Chain Considerations
Biologics manufacturers must provide a detailed and comprehensible description of the manufacturing method when applying for marketing authorisation. Producers of veterinary biologics are required to operate validated manufacturing processes and maintain rigorous in-process controls throughout development and commercial production. Furthermore, the manufacture of biologics must take place in facilities that are certified to GMP standards. These requirements ensure batch-to-batch consistency and safeguard product quality, which is central to regulatory approval and commercialisation.

Great Britain
Post-Brexit divergence requires strategic planning for commercialisation of veterinary biologics in the UK. Great Britain (GB) is governed by the Veterinary Medicines Regulations 2013 (UK VMR). Under UK VMR, veterinary biologics require a national GB MA. GB accepts applications supported by Annex II-type data and applies flexibilities for novel therapies. By contrast, Northern Ireland (NI) remains aligned with the EU VMR through the Windsor Framework. Biologics marketed in NI therefore required centralised EU authorisation or a national NI authorisation aligned with the EU data standards. A single EU-wide authorisation no longer enables full UK coverage. Companies now require a dual regulatory strategy for GB and the EU (including NI). Consequently, early planning of MA applications and procedural considerations is essential to avoid launch delays.

Approval Routes for Biosimilars
A biosimilar is a biological medicine that is highly similar to an existing, approved biological medicine (the "reference



medicine") in the EU in terms of structure, biological activity, safety, efficacy, and immunogenicity. Biosimilar veterinary products can be approved under the hybrid procedure (Article 19 EU VMR).

In contrast, generic authorisation (Article 18 EU VMR) requires bioequivalence to a reference veterinary medicinal product. Importantly, a biosimilar is not considered a generic version of a biological medicine as the characterisation of biologicals is intrinsically linked to the raw and starting materials, production process, and controls, which are usually proprietary and not available to the biosimilar manufacturer.

Biosimilar veterinary products applications must go beyond the requirements of generic small-molecule drugs. Applicants are expected to conduct a robust comparability assessment, quality, safety, and efficacy studies appropriate to the molecule's complexity; and engage in consultation with the relevant regulatory and scientific authorities (e.g. under the oversight of European Medicines Agency/CVMP for veterinary biologics) to justify similarity and approve market authorisation.

EU / UK Summary

Biologics offer significant therapeutic and commercial potential – but their complexity brings regulatory and operational challenges. Ultimately, successful commercialisation in the EU and UK requires strong manufacturing and quality systems, early engagement with regulators, and coordinated strategies for the GB and EU markets. Companies that invest early in regulatory planning, process development, and market access strategies are best positioned to capture the growing opportunities in veterinary biologics.

REFERENCES

1. 21 U.S.C. § 151 et seq.
2. 9 C.F.R. § 101.2.
3. Id. Additional examples of products that act primarily through the immune system were included in a 2013 memorandum of understanding (MOU) and include certain forms of interferons, viruses, antiserums, diagnostics, immunomodulators, serum, and plasma for passive transfer. See Memorandum of Understanding Between CVB and FDA (executed Feb. 4, 2013, amended Aug. 9, 2024) [hereinafter, the 2013 MOU].
4. 61 Fed. Reg. 43483, 43484 (Aug. 23, 1996) (proposed rule).
5. 9 C.F.R. § 102.3; § 113.2; § 113.3.
6. 9 C.F.R. § 114.9; § 114.8.
7. 9 C.F.R. § 114.7; § 114.9; § 116.1–116.6.
8. 9 C.F.R. § 112.5; § 112.7.
9. 21 C.F.R. § 510.4.
10. 21 U.S.C. § 321(g)(1).
11. 2013 MOU.

Dr. Chris Boyle

Dr. Chris Boyle, Partner, Sidley Austin LLP, combines his qualifications as a veterinarian and life sciences lawyer to guide animal health companies through regulatory, compliance and litigation matters in animal health. He advises across the full lifecycle of veterinary medicines, devices, diagnostics, and feed, including in multi-jurisdictional projects. Chris founded and chairs Sidley Austin LLP's Animal Health Legal Forum, a platform for industry professionals to connect and discuss evolving legal and regulatory challenges.

Emily Marden

Emily Marden, Senior Counsel, Sidley Austin LLP, is trained in the life sciences and her practice focuses on regulatory and strategic questions across the development and lifecycle for innovative products, including complex drugs and biologics for human and animal populations, regenerative medicine and human and animal food, agriculture and dietary supplements. Emily also teaches at NYU School of Law and writes on topics relating to innovation.

Kevin A. Sforza

Kevin A. Sforza, Managing Associate, Sidley Austin LLP, advises companies in the human and animal food, agri-cultural, and life sciences industries on FDA and USDA regulatory matters, as well as AAFCO frameworks, product development and regulatory risk evaluation. He counsels clients throughout the product lifecycle on marketing authorisations, product classification, labeling and advertising and the safety and regulatory status of novel, biotechnology-derived and Generally Recognised as Safe (GRAS) substances.