Future veterinary drug approval in the European Union: a paradigm shift causing changes, challenges and opportunities

Thomas Heberer¹

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Veterinary medicine, and in particular the approval of veterinary medicinal products, will face far-reaching regulatory changes next year. The New Veterinary Medicines Regulation (EU) 2019/6 (NVR) becomes applicable on 28 January 2022. It repeals the Directive 2001/82/EC and it amends the provisions of Regulation (EU) 726/2004 relating to the authorization and supervision of veterinary medicines. This regulation currently governs the centralized marketing authorization procedure for both human and veterinary medicines. The NVR represents a paradigm shift as the authorization of medicinal products for human and veterinary use will be formally separated.

The NVR contains a number of new measures which shall increase the availability and safety of veterinary medicines, and is intended to enhance the EU's actions against antimicrobial resistance. The Federal Office of Consumer Protection and Food Safety (BVL), as the responsible German national competent authority for the authorization and registration of veterinary medicinal products both on the national and the European level, was strongly involved in the implementation process of the new Regulation. Employees of Department 3 (Veterinary Medicinal Products) of the BVL have worked and are still working in numerous national and European bodies on the further development of the NVR, including the respective delegated and implementing acts. At national level, the BVL supports the Federal Ministry of Food and Agriculture (BMEL), and at European level the European Medicines Agency (EMA) directly or indirectly through the Heads of Medicines Agencies (HMA), of which BVL is one of 40 national competent authorities. The EMA is working closely with the European Commission and the HMA in preparation for the implementation of the NVR. At the national level, the NVR is accompanied by a newly

designed national legislation. This is as well a paradigm shift, as the new national legislation will be separated from the existing National Medicines Act (AMG). Therefore, on national level veterinary medicinal products will be formally detached from medicinal products for human use, too.

The main objectives of the NVR are¹:

- to simplify the regulatory environment and to reduce the administrative burden for pharmaceutical companies developing veterinary medicines, e.g. by streamlined pharmacovigilance rules;
- to stimulate the development of innovative veterinary medicines, including products for small markets (veterinary limited markets);
- to improve the functioning of the internal market for veterinary medicines;
- to strengthen EU's action to fight antimicrobial resistance through specific measures, ensuring prudent and responsible use of antimicrobials in animals, including reserving certain antimicrobials for the treatment of infections in people.

The development of new central European databases is an essential but also challenging part of the NVR. These databases not only need to be developed, but will also be linked to existing or newly developed national databases in order to enable direct data exchange. A central component of this is the new Union Product Database (UPD), which must go live on 28 January 2022. These developments are also an essential building block for the future, a complete digitization of veterinary drug authorization and all subsequent or related processes.

As mentioned above, one of the main objectives of the NVR is to strengthen EU's action to fight antimicrobial resistance. To acquire solid and harmonized data on

✉ Thomas Heberer
thomas.heberer@bvl.bund.de

¹ Federal Office of Consumer Protection and Food Safety, Berlin, Germany

¹ Veterinary Medicines Regulation / European Medicines Agency <https://www.ema.europa.eu/en/veterinaryregulatory/overview/veterinary-medicines-regulation>. Accessed 11 November 2021

veterinary antimicrobial consumption in Europe, the regulation stipulates both the collection of sales and use data in all Member States. While sales data had already been collected in all Member States beforehand, the national implementation of use data collection is challenging. This will be initially conducted in 2023, comprising all major food-producing animal species. Following a step-wise approach, horses and other food-producing species will be included in 2026, and dogs, cats and fur animals at the latest in 2029. Several other important measures of the NVR and the new national regulation are helping to minimize the development of antibiotic resistance by restricting the use of antibiotics in animal husbandry. These comprise e.g. a list of antibiotics reserved exclusively for human medicine, and the restriction of the rededication of antibiotics. A sense of proportion is necessary here, as the treatment options for the administration of antimicrobials will be even more limited, but the possibility of animal treatment must continue to be guaranteed. The latter serves both animal health and animal welfare, but also human health by avoiding the spread of zoonosis. The successful fight against the spread of antibiotic resistance, which today is regarded as one of the greatest future challenges, can only succeed with the so-called One Health Approach (humans, animals and the environment). In Europe, strategies for this are currently being developed also based on the NVR. Here, the BVL has a leading role in designing the EMA/HMA Strategy 2020–2025 for the topic antimicrobial resistance.

Another area of significant changes are requests for variations of medicinal products. The Commission Implementing Regulation (EU) 2021/17 comprises a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and the Council. Any change not included in this list is considered as a variation requiring assessment. From our perspective, it is of great importance and therefore, pose a challenge to facilitate the process of these newly established types of variation on a routine basis, and most essentially to ensure that an efficient procedural approach will be maintained.

With the NVR as well as the national veterinary regulation coming into force in January 2022, the BVL will take over the responsibility for the approval of applications to conduct clinical trials. Since the conduct of clinical trials in Germany has so far been only noted to the federal state authorities, but did not need an approval, the development and implementation of this process is a major challenge for the BVL. However, the process of approval of clinical studies must not be seen as a bureaucratic obstacle but rather as a win–win-situation: the pharmaceutical companies receive scientific advice helping to not perform an expensive clinical

trial that is not appropriate for the application for authorization of a veterinary drug, whereas the BVL does not need to assess clinical studies that are inappropriately designed and/or performed in the later process of veterinary drug authorization.

The NVR not only introduces changes to the authorization process and status of veterinary medicinal products but also to the area of pharmacovigilance. While it is a big change that marketing authorization holders (MAHs) will now report suspected adverse events directly to the European pharmacovigilance database and no longer to the national competent authorities, the biggest change is the shift from the submission and assessment of periodic safety update reports, which will no longer be required, to the signal management process being the main tool for post-marketing surveillance of veterinary medicinal products. As part of the signal management process, implemented for ensuring a continuous and standardized surveillance, MAHs will now be required to submit for each of their veterinary medicinal products a yearly statement on the benefit-risk-balance to the European pharmacovigilance database. It will be the task of the competent authorities of all Member States in the European Union, in Germany the BVL, to establish a process that enables the assessment of these statements and to assess these submissions.

The BVL was and still is very interested in informing all stakeholders about the changes to the new legal regulations, and has already done so in several events.

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