For ill creatures great and small

***Anja Holm**, CVMP Chair, discusses striking the right balance between scientific detail and pragmatism when authorising veterinary medicines. Interview conducted by* **Dr med vet Birgit Roser**

***Q:* Could you tell our readers a bit about your background, what attracted you to the regulatory arena and how you came to join the Danish Health and Medicines Authority (DHMA)?**

A: I graduated in veterinary medicine (DVM) from Copenhagen University in 1994 and worked in veterinary practice for four years. However, a student job at Lundbeck and an interest in pharmacology and immunology had sparked my curiosity about this field. In 1998, I took on a role at the Danish Medicines Agency as a clinical assessor of pharmaceuticals and vaccines. The job covered the development of the veterinary side of our pharmacovigilance scheme, which introduced me to the European regulatory network and the interesting work coordinated by the European Medicines Agency (EMA).

After a number of years as a clinical assessor and pharmacovigilance expert, and a year in DNA vaccine research, I became the Danish member of the EMA's Committee for Medicinal Products for Veterinary Use (CVMP) in 2004. As a member of the Committee, I have been Rapporteur for several products in the centralised procedure, leading a team of assessors and the discussion to final conclusions. Over the years, I have added education in regulatory science, communication, negotiation and management to my academic qualifications to meet the expectations in a constantly developing job.

***Q:* What does your current role involve, and what are your favourite aspects of this role?**

A: As Chief Advisor in the Department of Medicines Authorisation and Availability, I have a broad range of responsibilities. The main role is as Chair of CVMP, of course, and that occupies most of my workdays with interesting and challenging scientific and strategic issues. As CVMP Chair, I also represent EU regulators in the Steering Committee for the Veterinary International Conference on Harmonisation (VICH). I participate in the EMA's Scientific Coordination Board, in the CVMP's Strategic Planning Group and other coordinating and visionary roles, which I enjoy a lot. For the Danish agency, I have been a member of the Danish Antibiotics Board since its inception, and of the European Surveillance Strategy (ESS) – a pharmacovigilance subgroup of the Heads of Medicines Agencies (HMA). In addition, I am the so-called national training champion for assessor training, which gives me the opportunity to use my broad experience and have many rewarding contacts both inside and outside the agency.

***Q:* You have been the CVMP Chair since 2010 – could you explain what your main role is on this Committee?**

A: Together with the EMA secretariat, I prepare and run the committee meetings where we discuss the assessment reports for new product applications, variations, referrals, etc, and adopt guidelines, reflection papers and regulatory decisions. A specific veterinary field is the evaluation of food safety for consumers of animal products like meat and milk, after the animal has been treated with medicines. This is a separate toxicological and exposure assessment resulting in a maximum residue level (MRL) for each substance, so the farmer can be sure he does not deliver unsafe milk or meat. The environmental risk assessment for veterinary medicines is also a lot more complex than for human medicines, because animals may be raised and treated directly in the environment.

The committee consists of more than 30 highly skilled and experienced members from the EU member states, who meet for three days every month. My job is to lead the discussions, uncover any differences in opinion, facilitate solutions and compromises and finally reach a decision or vote. This process is challenging, exciting and very interesting, also because we work with all the novel therapies and concepts developed by companies for the veterinary field, and because we have to handle the referrals where we must take a common EU decision on products for which national member states have expressed diverging views. Striking the right balance between scientific detail and pragmatism, between different cultures, opinions and personalities can be hard work and requires concentration, endurance and good humour to overcome the differences in a friendly atmosphere. The enthusiasm, knowledge and efforts invested by the committee members are impressive and I never stop admiring the capacity and dedication of these busy people. The CVMP also has ten working parties – two of them joint with the Committee for Medicinal Products for Human Use (CHMP) – and we task them to develop guidance and other documents in their relevant scientific or regulatory field. Progressing the committee and specific areas of importance requires strategic thinking, exchanges and reflections to keep the focus and momentum in our work. It is my last year as Chair, and I am grateful to have received the trust and support of the CVMP members and the incredible help of the EMA secretariat over the past five years.

Q: How is the CVMP affected by the increasing requirements for transparency in regulatory processes?

A: The EMA's transparency policy requires that the agendas and minutes of the CVMP's meetings are published and generally we see no problem in that. However, the text is carefully written because companies have legitimate commercial interests in keeping their projects confidential until the marketing authorisation (MA) is granted. We are also very aware that our assessment reports are scrutinised around the world, so they must be clear, consistent and scientifically robust with balanced decisions resting on our legal basis. One of my main priorities is to increase the transparency and predictability of the committee's decisions, because companies should be able to direct their investments to the right studies and projects to ensure their product applications will be successful in the end.

Q: What do you expect from the upcoming new veterinary medicines legislation? How does this impact on the work of the CVMP, and how do you feel it is affecting industry?

A: The European Commission aims for a complete revision of the legislation to ensure that a lot of the administrative burden is relieved from industry, for example by deleting the requirement for periodic safety update reports (PSURs) and renewals. The centralised procedure will be opened to all new products, whether novel, standard or generic, and an enormous initiative has been proposed to harmonise all existing summaries of product characteristics (SPCs) across similar products. On the other hand, limitations in authorisation and use of certain antibiotics, stricter requirements for the 3Rs (reduction, refinement and replacement of animal trials) compliance and decreased involvement of member states in assessment is also part of the proposal. If I worked on the human side, I would keep an eye on the development of this piece of legislation. There is also serious concerns expressed on the sustainability of the system and the workload transferred to the competent authorities, in particular since the resources on the veterinary side are so much less. The new veterinary legislation is an extremely essential tool for us, for the veterinary society, agriculture and for the pharmaceutical companies, and it is of utmost importance that we strike the right balance now.

Q: What is the average length of time it takes the CVMP to assess marketing authorisation applications (MAAs) and approve applications, variations and renewals?

A: The CVMP and the EMA's secretariat always keep to the timelines given in legislation, ie, 210 days for an MAA excluding the clock stop, and we know that predictability of the procedures is necessary for company planning. However, if an application is submitted prematurely with outstanding issues which need further documentation or explanation, then there may be long clock stops in the procedure, so that the applicant can improve the dossier to fulfil the requirements. The better the dossier, the smoother it goes through the assessment process. Therefore I think that more companies should make use of the scientific advice option – and follow the advice they get – because that will definitely reduce the risk for refusal or the request for additional late studies and delays.

Q: What do you see as the biggest challenges facing the CVMP in the next five years? What are your key objectives?

A: The new legislation and the potentially huge workload on the CVMP will be a major challenge. This relates not only to the increased assessment work on new products or on existing products that would be up for harmonisation, but also the impact from changing guidelines, referral procedures and international work.

The topic of antimicrobial resistance has been in focus for many years now and the CVMP has already done a lot in this field, and this will continue to be high on the agenda for many years to come. The environmental risk assessment and the focus on potentially long-term harmful substances is a challenge that is increasing in several EU agencies at present.

Improving availability of products for minor use and minor species (MUMS) in the veterinary field is one of my key objectives, because there is a high need for authorised products for species like ducks, rabbits and goats.. The unmet treatment needs relate to several factors, eg, the many different animal species with their individual diseases and production systems, geographical diversity in disease distribution across the EU, the need for adequate food safety and environmental safety and the cost of studies, authorisation and surveillance relative to the expected return on investment for the MA holder. The CVMP will continue to work to extrapolate MRL values to more species where possible, and to designate intended MUMS products to be eligible for reduced data requirements and even for financial incentives, such as free scientific advice and fee reduction if the product is for food-producing species.

Q: What have been the CVMP key successes to date? What have you been most proud of?

A: The transition to a highly efficient, professional scientific committee while keeping up with the increasing workload and complexity of products has been a major achievement over the years. In relation to antimicrobial resistance, the committee and its connected groups have made an enormous contribution to the regulatory input regarding prudent use of antibiotics in veterinary medicine. Over the past five years, more than eight guidelines and reflection papers have been published and more than 20 referrals related to antimicrobial products have been concluded, with increased collaboration established with the Commission, the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA), the World Organisation for Animal Health (OIE), and the World Health Organization (WHO) in this area.

Likewise, I am particularly proud of the successful and respectful cooperation we have developed, involving many different scientists with profound expertise in their fields and competent assessor teams.

The promotion of structured workplans and strategies for projects outside our normal business has made it possible to keep these many projects organised and reaching their goals. For example, the development of the benefit–risk concept for the veterinary field, the injection-site issue, advancing the 3Rs initiative, structuring our input and influence on the international discussions on antimicrobial resistance, and moving towards more proactive management of novel therapies and scientific advice... to name but a few!

Q: What do you think will be the most important issues the CVMP will face in the next five years?

A: Increased global cooperation, the new legislation and prudent use of antimicrobials are easy suggestions. For many other issues, it is difficult to answer because the content of the work with authorisation of new medicines relies on company plans. It requires both in-depth and widespread scientific knowledge from the assessors, who have to be up to date in several academic fields so they can match the level of the industry and deliver a critical and robust assessment. It

"I hope that companies will use the option of scientific advice more often, so that dossiers will be complete from day one"

is of course challenging to maintain this position and the European regulatory network has recently started an initiative to coordinate the training of assessors between agencies, which will influence the CVMP as well. It is also my hope that companies will use the option of scientific advice more often, so that dossiers will be complete from day one, the assessment will be straightforward and the applicant will avoid requests for new studies during the procedure.

Q: If you could change one thing about the CVMP tomorrow, what would it be?

A: I would grant CVMP members all the time and support from their home offices that they could dream of! Having said that, it is a privilege to have a job where every week offers new insights and where it is possible to influence the direction of development for veterinary medicinal products in the EU. Even more than that, it is a privilege to work together with so many highly professional people, who are so good at what they do. After each CVMP meeting, I look back over the decisions we have made and the progress during the meeting and it is crystal clear that cooperation improves the outcome. The results that the committee achieves together are much better than the sum of what we could do individually.

Q: On a professional level, who has influenced you most, and why?

A: On a professional level, Professor Christian Friis from the veterinary faculty in Copenhagen was an inspiring (and tough) teacher in pharmacology and toxicology when I was a vet student. I have been lucky to be able to draw on his enormous insight in this field when I started at the CVMP, and through all the years of his long membership on the committee. We have shared many interesting talks and good laughs over the tables at the EMA and I thank him for showing me how to cut straight to the core of the matter.

On a career level, Jytte Lyngvig, the former Director of the Danish Medicines Agency, has been an inspiring leader to follow. I always enjoyed watching her navigate to advance a topic and interacting in groups, where she worked constantly for the benefit of the employees and the responsibilities of our agency. From her I learned that the better the dialogue, the better the chance of a good result – and that even a small agency can play a large role if we help each other through good dialogue.

Q: And finally, on a more personal note, what was the last book you read?

A: *The Organized Mind* by Daniel J Levitin. He explains the scientific background for how the human brain works in complex situations and how we can help it cope with the information overload in our modern world. It was a gift from my husband and I still wonder if he was trying to tell me something!