The AVC's General Assembly 2023 and Artificial Intelligence

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AVC, the Association for Veterinary Consultants[1], was set up in 1995 to provide a home for the community of independent and small-business regulatory specialists, covering the expertise-span from pre-clinical toxicology and field-trials to strategy and hands-on dossier management. The founding members, of whom I was one, included Alastair Kidd, the first President, who had recently retired from the UK's Veterinary Medicines Directorate, and a number of others established in their consulting careers after, in most cases, work in industry. The international membership has expanded to include ex-government vets, academics with consultancy careers, PR & communications experts, marketing strategists, and those working in broader biosciences. The main criteria are graduation as a veterinarian and independence. That independence has helped AVC become a trusted commentator, stakeholder group and advisor for many of the relevant regulatory bodies in Europe, including EMA and EFSA.

Each year, the General Assembly is held in a different country and, in addition to providing the forum for statutory business, there is relaxed socialising and the opportunity to hear invited speakers, from amongst AVC's members and from outside, addressing relevant topics. In October 2023 we gathered for our 28th GA in the warm and welcoming Mediterranean city of Nice, to mark also 10 years since taking up official residency in France. Four long-term members of the AVC enlightened the rest of the attendees, including some new members, on their careers as veterinarians, their independent consultancy and the lessons learnt: Bill Vandaele, a founder-member; Elinor McCartney, recently retired from her Spain-based consultancy Pen&Tec (now part of Argenta) and currently Secretary of AVC; Tim Rowan, who specialises in pre-clinical pharmaceutical development and the 3Rs; and the author of this article, who consults on emerging diseases and the intersection between animal-origin materials and products for humans.

Nice also provided the backdrop for a discussion of Artificial Intelligence in Digital Pathology and Veterinary Toxicology, a fascinating and deep-ranging paper given by invited guest Alain Piton of ALP Quality Systems, Sophia Antipolis France. The advent of Artificial Intelligence, AI, alarms many people, mainly about how we can ever again trust what we read and see. One can imagine that some day, perhaps soon, a dossier will arrive at a regulatory agency entirely constructed by AI with relevant and believable deep-fake visual documentation. At the same time, the concept of AI provides others with a new view of an innovative future.

Dr Piton began by emphasising the fundamental requirement that data, whatever their format and however they are produced, must be consistent, accurate, trustworthy, comprehensive, complete and reliable. GLP (Good Laboratory Practice) and OECD guidance documents are generally the foundation for such data in the regulatory arena. Digital Pathology relies on the computer and algorithm-aided analysis of digitised data from microscope glass slides. Accuracy begins with the image of the slide specimen and its automated scanning. Algorithms can be designed to recognise specific pathologies, changes

1 www.avc-eu.de

in cell appearance, size changes and other cell reactions, or specific immunohistochemical changes. Qualification of the image-scanning systems requires an expert pathologist to ensure that the results of image analysis accord with the nature of the known pathology, and the results of digital image analysis and direct visual reading tell the same story. Fully-GLP compliant Whole Slide Imaging systems require qualification of complex interlinked equipment systems, terabytes of storage space, archiving of slides, and a strong audit trail. The question is being asked, is a digitised slide a 'true' copy of the original glass slide and acceptable for regulatory purposes; the answer should be 'yes' provided that the scanner is properly qualified, the system is appropriately QC'd, the resolution of the reading screens is very high so that the visualisation of fine detail is as good as an experienced pathologist can achieve from conventional glass slides, and the digitised files comply with GLP and GDP regulations. However, this still does not mean that the original glass slides can be eliminated and only the digitised versions retained; this question is still under review.

The AI aspect is promising in terms of improving the accuracy, speed, and efficiency of diagnosis in Digital Toxicology. A critical aspect is preparation of the specimens for visual analysis, beginning with the barcoding to allow full traceability. Without a rigorous approach to selection, preparation and visualisation of the specimens, application of high-level imaging analysis will not be consistent and reliable. The use of advanced algorithms begins to move towards machine learning and AI when the programs are teachable by their own outputs. Nevertheless, training schemes involving human input are required to establish the framework of operation for an algorithm and develop the aspects of machine learning and a more integrated version of this, deep learning. Not least, expert pathologists are required to establish the quality and quantity of data needed to train the algorithms, and the criteria for competency validation. The whole process requires continuous human-operated QC of the machine-output and refining the training, if necessary re-training, the algorithm also requires human input, with review of outputs and decisions on false diagnoses triggering the process. The algorithms also need revising and retraining as new images, new visualisation methods and new observations on signals of pathology and toxicity come along. The use of such AI-based systems and regulations intersect because AI is a diagnostic tool on a par with device-associated software, but as yet there are no specific regulations concerning machine learning, deep learning or AI systems.

Dr Piton's presentation was a timely reminder that there are still open questions about this intersection of regulation and AI. EMA and the Heads of Medicines Agencies published their joint AI workplan in December 2023, covering the next 5 years[2]. It will complement the EU's AI Act 2023 and establish guidance tailored to the different spheres of application of AI in product regulation as well as research and review schedules. I am sure AVC will be returning to this very important topic in its GAs and consultation responses in future.

2 https://www.ema.europa.eu/en/news/artificial-intelligence-workplan-guide-use-ai-medicines-regulation