VetCAST meeting at ECCMID, Madrid, 21-04-18, 5pm – 6pm.

Attending: Peter Damborg (Uni. of Copenhagen), Ludovic Pelligand (RVC), Kees Veldman (WBVR), Pierre-Louis Toutain (RVC/Toxalim), Andrew Mead (RVC), Pierre Rouppert (bioMérieux), Ayla Hesp (WBVR), Beatriz Guerra (EFSA), Lina Cavaco (Uni. of Copenhagen), Carmen Torres (Uni. La Rioja), Elisa Parrilla (ThermoFisher), Kristyna Brozova (Erba Lachema), Farid el Garch (Vetoquinol), Priscilla Guerra (Uni. of Copenhagen), Stine Hoelgaard (Evidensia HBG Sweden), Ulrika Grönlund (Anicura HQ), Thomas Fritsche (Marshfield Clinic), David Paisey (ThermoFisher), Nicole Hunter (ThermoFisher), Dale Clash (ThermoFisher), Sakurako Marchand (bioMérieux), Karen Mullen (bioMérieux).

1. Welcome and status of the JPIAMR project (Peter Damborg)
   a. The VetCAST JPIAMR network project is nearing completion. Peter summarized briefly how we have accomplished the four main objectives of the project:
      ii. Roadmap to access and handle PK data: the SOP has been finalized, and is now published on the EUCAST homepage.
      iii. Training course on PK/PD and breakpoint determination: a successful course was held in Toulouse in September 2017, and a small follow-up course had been held in Uppsala in December 2017 + another follow-up course is scheduled for the EAVPT Congress in Wroclaw, Poland, June 2018.
      iv. Development of one clinical breakpoint: we have collected most data needed to set a clinical breakpoint for florfenicol in Pasteurellaceae (see points 3-5 below).

2. VetCAST position paper (Pierre-Louis Toutain)
   i. This paper addresses the VetCAST approach to establishing clinical breakpoints; it highlights some of the veterinary-specific challenges. After a long and difficult review process, the paper was finally published in Frontiers in Microbiology in December 2017:
   ii. The paper has been extensively both viewed and downloaded from the journal homepage since publication (>1200 views, >300 downloads)
   iii. The paper is Open Access and is also linked to on the EUCAST homepage.

3. Collection of PK data (Ludovic Pelligand)
   a. Florfenicol PK data. A PK/PD breakpoint has been proposed by VetCAST using Monte Carlo simulation, based on PK data from approximately 50 calves representing 3 separate studies.
   b. Tetracycline PK data. At this time, we only have data for 10 calves from a study by Peter Lees. We have tried unsuccessfully to obtain additional PK data from the literature, the FARAD database, and pharmaceutical companies. More PK data are needed to establish PK/PD breakpoints.
   c. Fluoroquinolone PK data. Ludovic has asked a few pharmaceutical (pioneer and generic) companies for individual PK data in dogs. Responses have been received but no data so far.
4. Collection of MIC data (Kees Veldman)
   a. Kees presented the collected MIC data, which primarily comprises tetracycline, as this drug was the first one in focus.
   b. In the last year, the principal focus changed to florfenicol; a good quantity of florfenicol MIC data has been gathered from VetCAST members and from CEESA publications. Based on these data, the following ECOFFs will soon be proposed to EUCAST (NB: data yet to be validated):
      i. *Actinobacillus pleuropneumoniae* (proposed ECOFF=8 g/L),
      ii. *Mannheimia haemolytica* (proposed ECOFF=2 g/L),
      iii. *Bordetella bronchiseptica* (proposed ECOFF=0.5 g/L)
   c. The criteria and methods used to establish ECOFFs were presented (Eyeball method and ECOFFinder). Tentative ECOFFs (=TECOFFs) will be considered using less stringent criteria when only small MIC data-sets are available.
   d. Prospective MIC data collection will be facilitated by the new project IMPART (see point 7)

5. Introduction to VetCAST position paper and new florfenicol CBPs (Pierre-Louis Toutain)
   a. Overall, VetCAST has decided to use Time>MIC and AUC/MIC, but not Cmax/MIC as PK/PD index. For long-acting drugs, we will use only AUC/MIC as is currently the practice of EUCAST.
   b. Florfenicol
      i. Using a model developed by Lena Friberg, it was decided to use AUC/MIC as the best PK/PD index to correlate with outcome.
      ii. Probability of target attainment (PTA) analysis: the PK/PD cut-off was determined to be 1 µg/ml.
      iii. Based on this cut-off and the florfenicol ECOFFs (see point 4 above), we need to set a CBP. Ideally, clinical efficacy data should be used to support the decision of a CBP, but it is uncertain if such data are available. Furthermore, the decision process to reach CBPs should be formalized in a publicly available rationale document / SOP, as is the case for EUCAST. Such a document is currently being drafted by the SC.

6. Which breakpoints should be prioritized next? (Ludovic Pelligand)
   a. General speculation on how to prioritize CBPs in the future:
      i. We can review missing CBPs in CLSI-VAST.
      ii. We can ask what clinicians need and propose.
      iii. We can note which PK data are available and then use that.
   b. Potential new breakpoints
      i. Azalides for treatment of food animals. There are available PK data required to determine CBPs, but there is an unsolved issue concerning the fact that MICs in serum are much lower than in broth. For example, for tulathromycin there can be up to 50-fold difference for *M. haemolytica* and *P. multocida*. VetCAST is considering a sort of scaling factor to overcome this issue.
      ii. Amoxicillin for injection and oral use in pigs: most PK data needed to propose CBPs are available.
7. **VetCAST collaborations + funding options**
   a. EMA: the Steering Committee (SC) is in contact with EMA. Although EMA cannot fund VetCAST, our EMA contact person has promised to draft how the working relationship will function.
   b. DG Sante. CVOs from 4 EU countries have contacted DG Sante requesting support for VetCAST.
   c. A recently commenced Horizon 2020-funded project on phenotypic resistance ("IMPART") incorporates activities relevant to VetCAST, including setting of ECOFFs. Kees Veldman from the VetCAST SC is the coordinator.
   d. Other VetCAST-related networks/projects are currently running, and more have recently been applied for by members of the SC.
   e. In 2019, a new JPIAMR call on AMR surveillance will be launched. This is likely to be relevant for VetCAST.

8. **Any other business**
   a. Thomas Fritsche mentioned that several new CBPs will be released later this year by CLSI-VAST.

/Peter Damborg