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Subcommittee on Veterinary Antimicrobial Susceptibility Testing
Hyatt Regency Baltimore
Baltimore, Maryland, USA
21-22 June 2013

Summary Minutes

A meeting of the Clinical and Laboratory Standards Institute (CLSI) Subcommittee on Veterinary Antimicrobial Susceptibility Testing (VAST) was held on 21-22 June 2013 at the Hyatt Regency Baltimore Hotel in Baltimore Maryland. The following were in attendance:

Mark G. Papich, DVM, MS **Chairholder**	**North Carolina State University**
Shabbir Simjee, PhD **Vice Chairholder**	**Elanco Animal Health**

Members Present

Mike Apley, DVM, PhD	Kansas State University
Virginia R. Fajt, DVM, PhD, DACVCP	Texas A & M University
Cynthia C. Knapp, MS	Thermo Fisher Scientific
Markus Rose, DVM, PhD	Intervet Innovation GmbH
Stefan Schwarz, DVM	Friedrich-Loeffler-Institut (FLI)
Maria M. Traczewski, BS, MT(ASCP)	The Clinical Microbiology Institute
John D. Turnidge, MD	SA Pathology At Women's and Children's Hospital
Jeffrey L. Watts, PhD, RM(NRCM)	Pfizer Animal Health
Ching Ching Wu, DVM, PhD	National Taiwan University School of Vet Medicine

Advisors Present

Donald J. Bade, BS	Microbial Research, Inc.
Steven D. Brown, PhD, ABMM	The Clinical Microbiology Institute
Joshua Hayes, PhD	FDA, Center for Veterinary Medicine
Henry S. Heine, PhD	Institute of Therapeutic Innovation
Robert P. Hunter, MS, PhD	Elanco Animal Health
Brian V. Lubbers, DVM, PhD, DACVCP	Kansas State Veterinary Diagnostic Laboratory
Marilyn N. Martinez, PhD	FDA Center for Veterinary Medicine
Ron A. Miller, PhD	FDA Center for Veterinary Medicine
Lori T. Moon, MT(ASCP)	MSU Diagnostic Center for Population & Animal Health
Ian Morrissey, MBA, PhD, FRSM	IHMA Europe Sàrl
Thomas R. Shryock, PhD	Elanco Animal Health
Peter Silley, PhD	MB Consult Limited
Michael T. Sweeney	Pfizer Animal Health

Reviewers Present

Maureen K. Davidson, PhD	FDA Center for Veterinary Medicine
Scott B. Killian	Thermo Fisher Scientific
Xian-Zhi Li	Heath Canada Veterinary Drugs Directorate
Yuqing Liu	Shangdong Academy of Agricultural Science

Maureen Mansfield	Thermo Fisher Scientific
Bernd Stephan, PhD	Bayer Animal Health GmbH
S. Steve Yan, PhD	FDA Center for Veterinary Medicine

Observers Present

Pete Borriello, PhD FRCPath	Veterinary Medicines Directorate Woodham Lane
John Dallow	Quotient Bioresearch
Marit Maaland	University of Copenhagen Stigbojlen 4
Patrick Mcdermott, PhD	FDA Center for Veterinary Medicine
Karen Mullen	bioMerieux

CLSI Staff Present

Tracy Dooley, BS, MT(ASCP)	CLSI
Jenny Sarkisian, MLS(ASCP)^{CM}	CLSI

Opening Remarks

Dr. Papich began the meeting on Friday, 21 June at 8:00 am. He stated that the purpose of the meeting is for the sponsors to present data and the working groups to address their agenda item topics and obtain input from the subcommittee. During this time, the subcommittee will make motions and vote on the agenda topics.

Meeting Discussion

Following are the substantive discussion points of the meeting (See Table)

<table>
<tr><th colspan="2"></th><th>Agenda Topic</th></tr>
<tr><th colspan="2">Committee Discussion Points</th><th>Rationale for Decisions Made and/or path Forward</th></tr>
<tr><td>1.</td><td>CLSI Document Status Updates</td><td>
New Vet document Codes
<table>
<tr><th>Former Document Code</th><th>New Document Code</th><th>Document Title</th></tr>
<tr><td colspan="3">Veterinary Medicine</td></tr>
<tr><td>M31-A3</td><td>VET01-A3</td><td>Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals; Approved Standard—Third Edition</td></tr>
<tr><td>M37-A3</td><td>VET02-A3</td><td>Development of In Vitro Susceptibility Testing Criteria and Quality Control Parameters for Veterinary Antimicrobial Agents; Approved Guideline—Third Edition</td></tr>
<tr><td>M42/M49-S1</td><td>VET03/VET04-S1</td><td>Performance Standards for Antimicrobial Susceptibility Testing of Bacteria Isolated From Aquatic Animals; First Informational Supplement</td></tr>
<tr><td>M42-A</td><td>VET03-A</td><td>Methods for Antimicrobial Disk Susceptibility Testing of Bacteria Isolated From Aquatic Animals; Approved Guideline</td></tr>
<tr><td>M49-A</td><td>VET04-A</td><td>Methods for Broth Dilution Susceptibility Testing of Bacteria Isolated From Aquatic Animals; Approved Guideline</td></tr>
<tr><td>X08-R</td><td>VET05-R</td><td>Generation, Presentation, and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin; A Report</td></tr>
</table>
Recently Published CLSI Documents

<u>Published December 2012</u>

M54-A, Principles and Procedures for Detection of Fungi in Clinical Specimens – Direct Examination and Culture; Approved Guideline

M27-S4, Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Fourth Informational Supplement

M100-S23, Performance Standards for Antimicrobial Susceptibility Testing; Twenty Third Informational Supplement

<u>Published July 2013</u>

VET01-A4 and S2 Supplement, Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals
</td></tr>
<tr><td>2.</td><td>Interpretive Criteria for Gamithromycin for Bovine Respiratory Disease

Presenters:
Dr. Tessman
Dr. Widener</td><td>
Drs. Tessman and Widener presented data for MIC and disk diffusion breakpoints of Gamithromycin for cattle for Mannheimia haemolytica, Pasteurella multocida, and Histophilus somni. Based on the data presented, the following interpretive criteria were proposed:
<table>
<tr><th rowspan="2">Antimicrobial Agent</th><th rowspan="2">Disk Content</th><th colspan="3">Zone Diameter (mm)</th><th colspan="3">MIC breakpoint (ug/mL)</th></tr>
<tr><th>S</th><th>I</th><th>R</th><th>S</th><th>I</th><th>R</th></tr>
<tr><td>Mannheimia haemolytica
Pasteurella multocida
Histophilus somni</td><td>15 ug</td><td>≥15</td><td>12-14</td><td>≤11</td><td>≤16</td><td>32</td><td>≥64</td></tr>
</table>
</td></tr>
</table>

		Motion: The motion was to table discussion and vote. **Vote:** Passed (6 – approve, 2 – reject, 1 – abstain) The VAST Subcommittee tabled the proposed data and asked the sponsor to present additional data in the January 2014 meeting for further consideration. The following additional data was requested: • metabolism studies • differences between control and treatment • no excretion, activity data • deep justification on PK/PD studies • M37 requests in presentation • values of variability estimates • target variability • epidemiological cut-off • clinical cut-off • break out data by label claims
3.	**Interpretive Criteria for Pradofloxacin** Presenters: Dr. Silley Dr. Stephan	Drs. Silley and Stephan presented data for MIC and disk diffusion breakpoints of Pradofloxacin for dogs (dermal, UTI) for *Staphylococcus pseudintermedius* and *Escherichia coli*; and for cats (dermal, respiratory) for *Staphylococcus pseudintermedius*, *S. aureus*, *S. felis*, *Pasteurella multocida*, *Escherichia coli*, and *Streptococcus canis.* 1st Motion – to accept the breakpoints as presented. Motion not carried because there was no second. 2nd Motion – Accept the breakpoints with "*Staphylococcus* spp." instead of spelling each out/ Vote: Failed (0- approved, 9 – rejected) Motion 3 - Based on the data presented and much discussion, the following interpretive criteria were proposed to add to Table 2 of VET01:

Antimicrobial Agent	Disk Content	Zone Diameter (mm)			MIC Breakpoint (µg/mL)		
		S	I	R	S	I	R
Pradofloxacin							
Dogs (Dermal, UTI)	5 µg	≥24	20-23	≤19	≤0.25	0.5-1	≥2
Staphylococcus pseudintermedius							
Escherichia coli							
Cat (Dermal, Respiratory)	5 µg	≥24	20-23	≤19	≤0.25	0.5-1	≥2
Staphylococcus pseudintermedius, S. aureus, S. felis							
Escherichia coli							
Pasteurella multocida		≥24	-	-	≤0.25	-	-
Streptococcus canis (include S only comment)							

S only comment will read as "The susceptible only category is used for populations of organisms (usually one species) for which regression analysis (disk vs. MIC) cannot be performed. This breakpoint will permit detection of strains with decreased susceptibility as compared to the original population."

Vote: Passed (7 – approved, 2 – rejected)

<table>
<tr>
<td>4.</td>
<td>MIC QC for Avilamycin

Presenter:
Dr. Brown</td>
<td>Dr. Brown presented quality control study data for MIC testing of Avilamycin against E. faecalis ATCC® 29212 and C. difficile ATCC® 700057 on MH Broth Media. Based on the data presented, the following QC ranges were proposed:

<table>
<tr><th>Organism</th><th>Proposed QC Range (MIC (µg/ml))</th><th>Vote</th></tr>
<tr><td>E. faecalis ATCC 29212</td><td>0.5 - 2</td><td rowspan="2">Passed (8 – approved; 1 – rejected)</td></tr>
<tr><td>C. difficile ATCC 700057</td><td>0.03 – 0.25 (Rangefinder Method)</td></tr>
</table>
</td>
</tr>
<tr>
<td>5.</td>
<td>Disk Diffusion QC for Tylosin (15 µg and 30 µg QC Ranges)

Presenter:
Dr. Schwarz</td>
<td>Dr. Schwarz presented quality control study data for Disk Diffusion testing of Tylosin against Staphylococcus aureus ATCC® 25923 on plain Mueller-Hinton agar. Based on the data presented, the following QC ranges were proposed:

<table>
<tr><th>Organism</th><th>Disk Content</th><th>Proposed QC Ranges (mm)</th></tr>
<tr><td>S. aureus ATCC® 25923</td><td>30 µg</td><td>18 - 26</td></tr>
</table>

Motion: Remove the entire 60 µg disk content of Tylosin from Table 4 and add the QC range for the 30 µg disk content as stated above.
Vote: Passed (8 – approved, 0 – rejected, 1 – abstain)
</td>
</tr>
<tr>
<td>6.</td>
<td>Disk Diffusion QC for Cefoperazone (30 µg QC Ranges)

Presenter:
Dr. Schwarz</td>
<td>Dr. Schwarz presented quality control study data for Disk Diffusion testing of Cefoperazone against Staphylococcus aureus ATCC® 25923 and Escherichia coli ATCC® 25922 on plain Mueller-Hinton agar. Based on the data presented, the following QC ranges were proposed to be added to Table 4:

<table>
<tr><th>Organism</th><th>Proposed QC Ranges (mm)</th><th>Vote</th></tr>
<tr><td>Staphylococcus aureus ATCC® 25923</td><td>23 - 34</td><td rowspan="2">Passed (8 – approved, 0 – reject, 1 – abstain)</td></tr>
<tr><td>Escherichia coli ATCC® 25922</td><td>24 – 33</td></tr>
</table>
</td>
</tr>
<tr>
<td>7.</td>
<td>Interpretive Criteria for Canine Doxycycline</td>
<td>Dr. Papich gave a short introduction which included information on the currently available doxycycline formulations (approved in Europe, South Africa, Australia and New Zealand) and the recommended dosages for dogs and cats. Dr. Papich pointed towards the high protein binding in dogs (>91%) and the effects this has on the doxycycline total plasma concentration versus doxycycline unbound plasma concentration.

Concerning the interpretive criteria, Dr. Papich referred to Table 2 in the CLSI document Vet01-A3 where it is stated in the Comments column “Tetracycline tested as the class representative for susceptibility to chlortetracycline, doxycycline, minocycline, and oxytetracycline. Organisms that are susceptible to tetracycline are also considered</td>
</tr>
</table>

		susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline or minocycline or both." As there are no specific breakpoints for doxycycline, the aim of the present approach was to determine the interpretive criteria for doxycycline against bacterial isolates from dogs and in the future, also for cats and horses. Dr. Papich reviewed the currently available literature on doxycycline MICs by showing MIC distributions from Weese et al (2012), Ganiere et al (2005) as well as recently determined data from Maaland & Guardabassi. A comparison with the tetracycline MICs done by Maaland & Guardabassi revealed that the doxycycline MICs were usually 1-3 dilution steps lower than the tetracycline MICs. Maaland & Guardabassi also provided scattergrams that showed the comparison of MICs versus zone diameters for both tetracycline and doxycycline. Dr. Papich also provided an overview of the pharmacokinetic data for doxycycline in dogs. Doxycycline concentrations in dogs simulated from 5 mg/kg q12h, oral application revealed a doxycycline total plasma concentration around 4 µg/mL and a doxycycline unbound plasma concentration slightly above 0.25 µg/mL. Based on Andes & Craig (2007), the pharmacodynamic parameter predictive of efficacy is the 24 hr-AUC in relation to the MIC. The 24-hr AUC/MIC parameter best describes the dose-response relationship independent of the dosing frequency. Free-drug AUC/MIC associated with a static effect is approximately 25, whereas free-drug AUC/MIC associated with a 2 Log_{10} reduction is approximately 50. Monte Carlo simulations were done with the following input parameters: MIC: 0.03 → 8 µg/mL; Dose: 5 mg/kg, oral, twice-daily. These simulations showed a target AUC/MIC of 25 can be reached with a certainty of 97% if the canine bacteria have an MIC of 0.12 µg/mL. This value may be considered as PK-PD Cutoff (CO_{PD}). After extensive discussions about the need of clinical efficacy data and the MIC distributions available from the published literature, Dr. Papich suggested the following recommendations: (1) Canine-specific doxycycline breakpoints of S ≤ 0.125, I = 0.25 and R ≥ 0.5 µg/mL. (2) Correlating doxycycline zone diameter breakpoints of S ≥ 25, I = 21-24 and R ≤ 20 mm. Additional recommendations referred to the use of tetracycline zone diameters and MICs as surrogates for doxycycline susceptibility tests. Although some participants suggested not to include such surrogate tests in Table 2 as this information may cause more confusion than benefit, the following recommendations were suggested: (3) Tetracycline 30 µg disks may be used as a surrogate for doxycycline disks: S ≥ 23, I = 18-22 and R ≤ 17 mm (4) Tetracycline MIC breakpoints as a surrogate for susceptibility tests: S = 0.25, I = 0.5 and R = 1 µg/ml **Motion:** Approve the following breakpoints and comments for inclusion in Table 2:

Antimicrobial Agent	Disk Content	Zone Diameter (mm)			MIC Breakpoint (µg/mL)			Comments
		S	I	R	S	I	R	
Tetracyclines								
Doxycycline Dogs (Skin & Soft Tissue Infections)	30 µg	≥25	21-24	≤20	≤0.12	0.25	≥0.5	Breakpoint derived from microbiological, and pharmacokinetic data using clinical dose of 5 mg/kg, oral, twice –daily, and pharmacodynamic data.
Staphylococcus pseudintermedius	30 µg (tetracycline)	≥22	18-22	≤17	≤ 0.25 (tetracycline)	0.5 (tetracycline)	≥ 1.0 (tetracycline)	Tetracycline may be used as a class representative for doxycycline. Report doxycycline susceptible or resistant based on the tetracycline result.

Vote: Passed (8 – approved; 0 – rejected; 1 – abstain)

8. Aquaculture Working Group Update

Chairholder: Ron A. Miller

Members: Jeremy Carson, Inger Dalsgaard, Patricia Gaunt, Charles Gieseker, John P. Hawke, Renate Reimschuessel, Peter R. Smith, Temdoung Somsiri, Ching Ching Wu

Dr. Miller gave an updated report on progress being made for:

- standard broth microdilution methods for *Flavobacterium coumnare* and *F. psychrophilum*
- Standard disk diffusion methods for fish pathogenic streptococci
- *Edwardsiella ictaluri* collaboration
- Anticipated research on *F. psychrophilum* and *E. tarda*
- Recently published work that the working group will consider the impact of the findings for the revision of VET-04 (M49) and using the data to set ECVs in the near future

9.	**Prospectus Mind the Gap** Chairholder: Tom Shryock Recoding Secretary: Henry Heine Members: Stefan Schwarz, Mark Papich	Dr. Shryock presented the current state of VAST committee and what some options are to move it to a Future State. The current state of the committee is to create and use guidelines with recommendations for culture and susceptibility testing to guide veterinarians in selection of appropriate antibiotics. However, not all antibiotics have breakpoints in VET-01; fewer new antibiotics are coming to VAST; VET-06 (M56) initiative is limited to available data; and antimicrobial resistance monitoring program reports need harmonization. He discussed some of the current gaps, such as the need to "VET-02 (M37A3) like" data, and types and quality of data. He also challenged the committee with proposals for a VAST Path Forward to address the issues. He recommended the following path forward: - Develop "prospectus", an action and benefits for research investment - Communicate the need to funding agencies - Inventory/matrix of data needs should be created - Prioritization for use in seeking external support - Other miscellaneous considerations (eg, involvement of veterinary organizations [AVMA]; publication; presentations; appropriate funding agencies) The WG group needs the following inputs from the committee: - Need to finalize matrix of needed information - Need to finalize key organization contacts - Input on approach and value
10.	**VET-06 (M56) Update** Co-Chairholder: Maria Traczewski Co-Chairholder: Mike Sweeney Members: Donald Bade, Tom Fritsche, Rob Hunter, Brian Lubbers, Patrick McDonough, Stefan Schwarz, Shabs Simjee, Vijay Singu, Ching Ching Wu	Ms. Traczewski reviewed the Comments Table on AST of Infrequently Isolated Bacteria From Animals (Vet06) based on subcommittee review of the initial draft to help finalize the document. **Comments from the subcommittee included:** Virginia Fajt: Some drugs may not be applicable in the Tables since they are for human health and won't be used in animal health. The WG needs to review and remove those drugs that won't be used. Peter Silley: How useful will the breakpoints be for the listed fastidious organisms? Breakpoints from human health don't mean anything and may lead to reader confusion. Suggest that you leave these out of the document. Lori Moon: Consider adding *Bibersteinia trehalosi* to document. Don Bade and Peter Silley: The purpose of this document is to describe and reference methodologies for testing fastidious organisms with antimicrobials so that breakpoints might be generated. A Methods-based document may lead to the eventual proposal of breakpoints from data generated by numerous labs that work with these fastidious organisms. If breakpoints for fastidious organisms do exist now, then we can still reference the methods and add those data. The overall focus of the first version of Vet-06 should be similar to the evolution of M45 with a methods/QC based

		document. JohnTurnidge: Would still like to see a version based on the original intent, that is, include proposed breakpoints with methods and QC and see if it's at a good enough quality to move forward. Brian Lubbers: Consider adding *Gallibacterium anatis* formerly *Pasteurella* to the document. **Overall Subcommittee recommendations**: Review tables and determine which drugs are not appropriate for this document and determine which veterinary breakpoints can be added. Decide what to do with methods that have no QC. **Actions**: (1) Go through tables to confirm that drugs are appropriate to list or replace with more appropriate drugs for organisms; (2) Discuss if breakpoints will be human health, vet health or both (or neither); consider a Methods-based document with no IC until future versions. (2) Add a table with list of species that we could not find enough data on to put a method in for the first version of the document. (3) The working group will schedule a teleconference in September to go through the current document for the purpose of eliminating drugs that are not used in veterinary medicine, to review where QC is lacking and to discuss a table that will list strains with some published methods but not enough to make it to a table in Vet-06. The goal of this meeting is to come up with Draft 1 to present to the subcommittee for a vote. All interested parties will are welcome to join the call.
11.	**X08 Update** Presenter: Shabir Simjee	Mr. Simjee, chairholder of the X08 Report published in September 2011 drafted a project proposal to move the X08 Report to a Guideline. During the VAST meeting, Dr. Simjee reviewed some of the comments the members and advisors had posed from the project proposal review, and the following were discussed (in particular the questions raised by the FDA): - In the project proposal it was stated that the Report should be moved to a Standard; however, it was brought up that the document will be proposed as a Guideline instead - There was a concern whether companion animals and also target pathogen animals should be included – decision was made to focus on targeted pathogens - This document is only meant to be for epidemiological purposes (monitoring and surveillance) - Will the ECV be the same as the wild type cutoff in VET02 (M37)?- yes it is the same parameter, just the wild type cutoff was never published in VET02 - Would the wild type cutoffs be used to address clinical breakpoints in VET-02 (M37) - What happens when data has a shift, how will that be handled; and will statistics be included?

		- Where is the date going to come from? – two surveillance programs: VetPath will provide published MIC distributions and German GermVet program, and then rely on publications - Due to limited time, and the fact that this is a proposal (not an actual Working Group to draft this), some of the questions are too specific for the subcommittee to address. Therefore, not all the comments were addressed. - The ECV's should not be published in M37 because it may cause confusion and be used for diagnostic purposed instead of monitoring purposes only. Therefore, a separate document needs to be published. - **Action:** Dr. Simjee will address the comments and then the revised proposal with the comments will be circulated back to the committee (members, advisors, reviewers, and guests from the June 2013 VAST meeting) for comment and approval. After the committee approves the proposal, it will then move to the consensus committee. Then the next step will be to form the committee.
12.	**Editorial Working Group** Chairholder: Mike Sweeney Recording Secretary: Maria Traczewski Members: Steve Yan, Jeff Watts, Mark Papich, Henry Heine, Markus Rose, Stafan Schwarz, Lori Moon, Ching Ching Wu	Mr. Sweeney presented to the committee different layouts for the Tables in VET01 (M31). The following was the discussion: 1. Table one possible modifications a. Table 1a—US b. Table 1b—Europe This would eliminate a lot of the comments WG will come up with some mockups for the next meeting. 2. Table 2 will become a list of susceptibility test methods 3. Table 3 will become the old table 2. Two options a. Tables divided by animal species,3, 4,5,etc…., cat,dog,swine, etc b. Tables organized by bacterial groups 3, 4, 5, etc…Enterobacteriaceae, Pseudomonas aerug., non-enterobacteriaceae,etc. Comments: IF the tables get listed by organism group, then methods and QC can be placed on top. Opinions: Lori Moon did a survey of lab managers at a recent meeting and found most wanted the tables listed by organism group. Brian Lubbers will be attending a conference this month and will solicit more opinions. Tom Fritsche recommended using the tables listed by animal species. Using the drugs in table 1 as a guide. Vet and pharmacology people liked the animal species listing better.

		There was also a discussion about the need for an affordable searchable/sortable document due the wide variety of opinions on Table 2. This will be considered in the future. Decisions: **Action**: CLSI staff will send out the examples to the entire group and get votes on which way to go. Once votes come in, the WG will begin to redo the tables accordingly for next supplement.
13.	**Proposal to Establish Veterinary-Specific Interpretive Criteria for Cloxacillin** Presenter: Mr. Sweeney	Mr. Sweeney asked the committee for guidance to establish interpretive criteria for cloxacillin (and oxacillin), to ensure it is worthwhile investing time and resources for this. He recommended that Zoetis work with the VAST Generic WG for the development of Veterinary Specific IC for cloxacillin (and oxacillin) for the label pathogens (*S. aureus*, and *S. agalactiae*) to demonstrate concentrations in milk above the MIC; activity for drug in the milk. The committee recommended the sponsor come with the milk residue data in January 2014 for the committee to decide how to proceed. A suggestion was made to use this to create a criteria into VET02 (M37) to specifically deal with mastitis indications in the future.
14.	**VFM Working Group** Chairholder: Don Bade Recording Secretary: Cynthia Knapp Members: Mark Papich, Shabs Simjee, Jeff Watts, Scott Killian, Cindy Lindeman, Maria Traczewski, Tom Shryock, Ching Ching Wu, Lori Moon	Mr. Bade presented the next set of testing data that was performed at 4 different testing labs evaluating more formulations of media that would not require the addition of supplement C for testing fastidious Gram- Negative veterinary pathogens. • Organisms: *Actinobacillus pleuropneumoniae* *Histophilus somni* *Haemophilus parasuis* • The latest testing formulations were : 1. MHF-Y 2. MHF-Y with FBS (fetal bovine serum) 3. BF-Y Brain heart infusion broth as the base instead of MHB 4. MHF-YBSA, bovine serum albumin 5. VFMY, additional yeast no supplement C • Results of testing: 1. BF-Y , was found to be unacceptable due to precipitation 2. MHF-Y, MHF-YFBS, MHF-YBSA, provided ok growth for all organisms 3. VFMY, did not provide adequate growth 4. MHF-Y produced similar results to the first round of testing but lower growth scores which may be due

		to different lots of yeast extract or MHB. 5. The only media that offered any support of growth to HP was MHF-FBS and it adequately supported both AP and HS in CO2. • Conclusion: 1. MHF-Y, MHF-YFBS, & MHF-YBSA are all candidates for replacement of VFM for AP and HS. The addition of FBS did not enhance the growth of AP or HS only HP. BSA did not add any value to the MHF-Y base. 2. FBS presents difficult shipping issues when trying to ship internationally. • Next Step, discussion on what direction we go: 1. MHF-Y, we need to prepare several batches of this media with different lots of yeast extract to look for any lot to lot variability. These will be made by each of the 4 labs and shared and tested at each site. After this media testing is completed and if successful we will then do a bridging study for QC testing with several drugs and compare the new media (perhaps multiple lots) to VFM as a control in the 4 testing labs.
15.	**Questions from FDA** Presenter: Dr. Martinez	Dr. Martinez presented and discussed questions the FDA has posed for the committee. 1. Will the SC allow veterinary-specific interpretive criteria (VSIC) be established and included on M31's Table 2 for antimicrobials without prior regulatory approval in any jurisdiction? (Clarification to the question - does it have to be a drug that has been approved (new drug?)) - QC data is required before a drug is added to Table 2 - All breakpoints are provisional for a year - If it has not yet been approved, there needs to be an indication that it is an investigational drug 2. How should we handle situations where different doses/dosage regimens/routes are approved across jurisdictions (resulting in potentially different VSIC)? and 3. Where should this dosage information be documented when establishing VSIC? - AST has addressed this issue by putting into the document that breakpoints are based upon a dosage regimen of "X" in the comments. So if any other country uses a different regimen, they will have to make a choice on what to do with the drug/bug combination in a particular species. - Recommendation: publish what the decision was based upon for all approved drugs going forward - More information is needed for international purposes (dose, regimen, etc) - How is the laboratorian supposed to know what dose the veterinarian is using? - Is this information better suited in the rationale document or in the comments section of the published document? - **Action**: Discussion in January on how to handle these types of situations

		4. Does the SC think that the cut-off values that are used in setting VSIC should be documented? If so, where should it be documented (eg, meeting minutes, comments section of M31's Table 2, an internal working document)? - This is being worked on. Current information is publicly accessible to the public from the CLSI website.
16.	**VET02 (M37) Updates** Chairholder: Marilyn Martinez Vice Chairholder: Rob Hunter Members: John Turnidge, Mark Papich, Peter Silley, Jeff Watts, Xian-Zhi Li, Markus Rose	Dr. Martinez gave an update on the progress of VET02 (M37) and indicated to the committee that there will be a lot to discuss in the January 2014 meeting based on the current progress. - VET02 revision is underway, Dr. Martinez and Dr. Turnidge are still going through the document to remove the existing redundancy. - Dr. Martinez and Dr. Turnidge are still evaluating the proposed approach to clinical cutoff values. They hope to have more information to present in January for the method proposal (how to establish it) and how the existing flow chart will change if COcl cannot be defined. - There are still points that remain undefined for PD cutoffs (eg, mastitis and macrolides) - After much discussion and work with Drs. Papich and Rose, the following proposal is being considered for Macrolide COpd for respiratory disease: o Measure PELF o Establish a relationship between PELF and blood levels o Estimate time above the MIC_{90} of the targeted pathogen in the PELF o Divide the mean AUC by that MIC_{90} o Do MIC Simulation to get the 90% TAR based upon blood concentration-time profiles
17.	**Education Working Group** Chairholder: Virginia Fajt Recording Secretary: Mike Apley Members: Bob Badel, Rob Hunter, Jennifer Lorbach, Mark Papich, Tom Shryock, Ching Ching Wu	During the regularly scheduled VAST meeting, the Education Working Group discussed the on-going progress for the following projects for the WG during 2013: 1. Create rationale documents for newly set breakpoints, with special emphasis on explaining the approaches used for generic drugs 2. Possibility of having Table 2 as a stand-alone item for purchase, which might be useful and marketable to veterinarians and educators 3. Complete the work on a manuscript that is designed to give advice to reviewers and researchers on performing and interpreting antimicrobial susceptibility testing (this manuscript is about 80% completed) 4. Begin work on a review article that would provide advice to clinicians about how to use and interpret antimicrobial susceptibility testing 5. Provide assistance with getting letters to editors and list servs when the larger committee comes up with a summary of the gaps in the research data that would assist us in setting breakpoints

19.	**Generic Working Group** Chairholder: Ching Ching Wu Reporting Secretary: Stefan Schwarz Members: Shabbir Simjee, Cindy Lindeman, Virginia Fajt, Mark Papich, John Turnidge, Marilyn Martinez, Rob Hunter, Tim Frana, Vijay Singu, Tara Bidgood , and Luca Guardabassi	Dr. Papich gave a short introduction in which he referred to a large data set provided by Dr. Frana for Amikacin. This data set includes Gram-positive and Gram-negative bacteria from dogs, horses and cats. Analysis of the data revealed that the vast majority of the *E. coli*, *Pseudomonas aeruginosa*, *Pseudomonas* spp. and *Staphylococcus* spp. isolates had MICs of < 4 µg/mL. The test range included only 4 concentrations (4, 8, 16 and 32 µg/mL). Hence the real MIC in the range below 4 µg/mL is not known. Dr. Papich also presented EUCAST MIC distributions for a wide variety of bacteria from human origin obtained with a wider test range. As there is no data for veterinary isolates and the MIC range is below 4 µg/mL, it was suggested to either rely on human data from EUCAST or to generate new data. For the latter aspect, several participants volunteered to test strains if microtitre plates can be provided. For this, Dr. Papich will get in touch with Dr. Knapp. Dr. Papich also provided an overview about pharmakokinetic data in adult horses based on 11 data sets. He also stated that there is virtually no protein binding of amikacin. Monte Carlo simulations for an input dose of 10 mg/kg in adult horses and 20 mg/kg in foals were shown. The Generics Working Group decided to postpone the amikacin work to the January 2014 meeting and hope that additional MIC testing may have been performed until then.

Next Meeting Reminder:

The next meeting of the Subcommittee on Veterinary Antimicrobial Susceptibility Testing will be scheduled as a two-day meeting on 9-10 January 2014, in San Antonio, Texas.

Adjournment

Dr. Papich thanked the participants for their attendance and input. The meeting was adjourned at 11:55AM.

Respectfully submitted,

Jenny Sarkisian, MLS(ASCP)^{CM}
Standards Project Manager