UPDATE ON NAHLN ACTIVITIES

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U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINARY SERVICES
NATIONAL ANIMAL HEALTH LABORATORY NETWORK
OCTOBER 2018
NAHLN Hot Topics

African Swine Fever Response
vNDV outbreak
Adding assays to NAHLN
NAHLN Coordinating Council update
NAHLN Methods Technical Working Group update
AMR Pilot update
African Swine Fever Response

- NAHLN included in a meeting with swine industry in Washington DC
  - NPB, NCCP, AASV, USDA-VS, FDA
  - Discussed prevention and response

- Letter from the VS Deputy Administrator with guidance for testing in NAHLN labs
  - Discourages unofficial testing for NAHLN scope diseases using unapproved assays and/or unapproved sample types
African Swine Fever Response

NAHLN:
- Survey 11 approved labs for current capacity- 6500 PCR tests/day
  - increase PT’d analyst – 8000 PCR tests/day

- Increase sample types for approved testing (FADI)
  - Tonsil- October 1, 2018
  - Spleen- December 1, 2018

- Increased the number of approved NAHLN labs
  - All labs have been asked for interest to participate

- Supporting discussions around active surveillance plan
  - Swine staff, CEAH, FADDL, NAHLN labs
Newcastle (vNDV) Outbreak

NAHLN Response

California Animal Health and Food Safety Laboratory (NAHLN Lab)

~ 13,000 PCR tests performed
  ◦ Messaging:
    ◦ CAHFS lab is messaging results

Laboratory capacity increased by adding administrative support from 2 other NAHLN labs
  ◦ Oregon Veterinary Diagnostic Lab
  ◦ Colorado State University Veterinary Diagnostic Lab
  ◦ Intergovernmental Personnel Act Assignment Agreement
Laboratory Electronic Messaging

43 NAHLN labs and NVSL are capable of sending an electronic message
• Additional 2-3 labs prepared to message

Messages now being received for 9 NAHLN scope diseases
• **ASF, BSE, CSF, FMD, IAV-A, IAV-S, vND, PRV, VSV**

Training offered to NAHLN laboratories and VS commodity staff
• Basic and HL7 specific messaging training
• LIMS Vendor specific training
• Training for commodity/program staff

2019 messaging priorities include:
• Continue to expand number of labs with capability to message
• Expand messaging to include Scrapie and AMR data
• Support implementation of NLRAD
• Integration with other internal VS systems
• Enhance utility of messaging standards
Adding a Disease/Assay to NVSL and NAHLN

Adding a disease program disease to NVSL:
- Need for a National oversight is identified
  - Determination if the disease should be under NAHLN scope
- Surveillance plan is developed
  - Active Surveillance
  - Passive Surveillance
- Proficiency test
- Funding

Adding a disease/assay to NAHLN scope
- Need identified for disease or assay to be added to NAHLN scope
- Proposal goes to the NAHLN Methods Technical Working Group (MTWG)
  - If accepted, the study is completed
  - Study results are presented to the NAHLN MTWG
    - MTWG makes a recommendation to NAHLN Coordinating Council (CC)
    - CC makes a recommendation to the NAHLN Executive Committee who either decides or takes the recommendation to the VS Deputy Administration if needed
  - If recommended- then VS determines how the assay may be incorporated into the NAHLN
Coordinating Council- Update

Welcomed 4 new members
- Dr. François Elvinger - Cornell Animal Health Diagnostic Center
- Dr. Brett Webb North Dakota State Veterinary Diagnostic Laboratory
- Dr. Larry Forgey; Missouri Department of Agriculture:
- Dr. Peter Mundschenk - State animal health official for Arizona

Laboratory Assessment Matrix
- Time line for implementation and changes for FY2020

NAHLN Strategic Plan
- Update of the plan- completion December 31, 2018
MTWG Update
Membership

**NAHLN Laboratories**
- Dan Bradway – WA
- Beate Crossley – CA
- Jane Hennings – SD
- Hon Ip – WI
- **Donna Mulrooney – OR***
- **Akhilesh Ramachandran – OK***
- Rachel Reams – MI (co-chair)
- Susan Sanchez – GA
- Jackie Smith – KY
- **Rebecca Wilkes – GA***
- Yan Zhang - OH

*new members as of January, 2018

**NVSL reference laboratories + NAHLN**
- Tracy Sturgill – FADDL
- Nita Grause – DBRL
- Beth Harris – NAHLN (Co-chair)
- Mary Lea Killian – DVL
- Aaron Lehmkuhl – DBPL
- Christie Loiacono – NAHLN
- Greg Mayr – FADDL
- Monica Reising – CVB
- Janet Warg - DVL
2018 Activities to Date

Methods Comparisons

- **FMD/CSF Testing**: Comparison of the Performance of the Applied Biosystems® 7500 Real-Time PCR System to the Applied Biosystems® QuantStudio 5 Real-Time PCR Detection System for the detection of FMDV and CSFV

- **FMD/CSF Testing**: Comparison of the MagMAX™ Pathogen RNA/DNA Kit, MagMAX™ CORE Nucleic Acid Purification Kit, and the Qiagen MagAttract 96 cador Pathogen Kit.

2018 Activities to Date

Other activities

- **MTWG Core meeting schedule**: proposed modification to move core calls to monthly (now bi-monthly), and move general MTWG calls to quarterly (now bi-monthly).
  - Needed to ensure MTWG Core goals accomplished in designated timeframe
- **PRV testing**: Sub-committee stood up to evaluate data from available PRV PCRs for potential deployment to the NAHLN
- **IAV-A testing**: Reviewed IDEXX avian influenza A RNA real-time PCR test and nucleic acid extraction kit
- **FMD/CSF Testing**: Identified need for low throughput kit for FMD/CSF
MTWG prioritized list of activities for 2018-2019

June face-to-face meeting

1. Evaluate WGS and metagenomics technology for deployment to the NAHLN [short term-survey; mid-long term-implementation]

2. Harmonize PCR thermocycling parameters [short-term]

3. Develop NAHLN communications plan [mid-term]

4. Continue to ID 2nd manufacturer for platforms and kits/reagents where feasible [long-term]

5. High priority situations – validate alternative sample types for NAHLN SOPs [long-term]

6. High priority situations – emergency validation of SOP for new disease [long-term]

7. New priority category for endemic look-alikes to FADs [short-term]

8. Share assays for endemic diseases across NAHLN [short-term]
NAHLN MTWG activity 2018-2019

- Evaluate WGS and metagenomics tech
- Develop NAHLN communications plan
- Validate alternative samples for high priority...
- New priority category for look-alikes to FADs
AMR Pilot Project

SUMMARY OF YEAR 1
Objectives

Develop process for tracking AMR data at a national level
- standardized methodology, interpretation, and reporting mechanisms.

Deploy across multiple laboratories

Identify information important to veterinary diagnostic community regarding trends in AMR
- facilitate antimicrobial stewardship.
## Pathogen/animal species – Year 1

<table>
<thead>
<tr>
<th>Bacterial pathogen</th>
<th>Animal Species</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>cattle, swine, poultry, horses, dogs, cats</td>
</tr>
<tr>
<td><em>Salmonella enterica</em></td>
<td>cattle, swine, poultry, horses, dogs, cats</td>
</tr>
<tr>
<td><em>Mannheimia haemolytica</em></td>
<td>cattle</td>
</tr>
<tr>
<td><em>Staphylococcus intermedius group</em></td>
<td>dogs, cats</td>
</tr>
</tbody>
</table>

*Includes *S. intermedius*, *S. pseudintermedius* and *S. delphini*.  

*
Measures of Success

Laboratories able to meet 50% or more of project’s target numbers in Year 1

VS can develop parameters for electronically messaging AST data
  ◦ at least 20% of laboratories able to successfully message AST data during Year 1

VS develop reporting mechanism to share results from Year 1 of this pilot with laboratories, State and federal regulatory authorities, and other interested stakeholders
Measures of Success - Target numbers

Summary of Testing

Laboratories able to meet 50% or more of project’s target numbers in Year 1

- E. coli - Cattle: 257
- Salmonella - Cattle: 248
- Mannheimia - Cattle: 248
- E. coli - Swine: 70
- Salmonella - Swine: 38
- Mannheimia - Swine: 21
- E. coli - Poultry: 171
- Salmonella - Poultry: 158
- Staph: 326
- E. coli - Dogs: 8
- Salmonella - Dogs: 387
- Staph - Dogs: 192
- E. coli - Cats: 3
- Salmonella - Cats: 30
- Staph - Cats: 30

Total isolates – 2191 (as of 10/4/18)

- 6 categories – already met goal of 200 isolates
- 3 categories – on track to meet goal by Dec 2018
- 7 categories – unlikely to meet goal of 200 isolates by Dec 2018
  - E. coli - swine
  - Salmonella/all animal categories except cattle
  - Staph – cats
Measures of Success – messaging data

VS can develop parameters for electronically messaging AST data

- HL7 messaging schema was developed for messaging AST results
  - Requirements of message structure – “all or none”. Cannot select which AST data to message if 2 or more in same accession.
  - Requirements of AMR pilot project – cannot attach accession number from original client submission to isolate. Message structure requires Accession # to be included.

Path Forward: Script written to convert data from spreadsheet into HL7 message, then send the message to the LMS database
Measures of Success – Reporting Mechanism

VS develop reporting mechanism to share results from Year 1 of this pilot with laboratories, State and federal regulatory authorities, and other interested stakeholders

Subcommittee stood up to identify recommendations for reporting data

Tableau software in development for creating interactive website to display data

Written report in development; estimated completion date – December 2018
Sub committee: AST Data Reporting Guidance

1. Report summary data across all laboratories, by animal species and bacterial pathogen

2. Report all MIC values obtained for all antibiotics on the plate
   ◦ Allows data to be evaluated for both therapeutic/clinical and epidemiological/surveillance applications

3. Only report breakpoints for antibiotics with animal-specific interpretive values

4. Report dog/cat UTI isolates separately

5. Report dog/cat Staph. OX-S and OX-R isolates separately
### Example: Cattle – *Mannheimia haemolytica*

Animal-specific interpretive criteria are indicated for selected antibiotics. Green shaded cells = sensitive, yellow shaded cells = intermediate and red shaded cells = resistant.

Interpretive values based on CLSI Vet08, 4th ed. (2018)

<table>
<thead>
<tr>
<th>Antibiotic Class</th>
<th>Antibiotic</th>
<th>MIC Value (ug/ml)</th>
<th>Total Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycoside</td>
<td>Gentamicin</td>
<td>&lt;=0.12 0.12 &lt;=0.25 0.25 &lt;=0.5 0.5 &lt;=1 1 &gt;1 2 &lt;=4 4 &lt;=8 8 &gt;8 16 &gt;16 32 &gt;32 64 &gt;64 &lt;=256 256</td>
<td>182</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>Neomycin</td>
<td>23 0 126 15 2 1 15</td>
<td>180</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>Sulphadimethoxine</td>
<td>99 0 29 2 2 48</td>
<td>184</td>
</tr>
<tr>
<td>Fluroquinolone</td>
<td>Danofloxacin</td>
<td>130 0 6 9 4 34</td>
<td>183</td>
</tr>
<tr>
<td>Fluroquinolone</td>
<td>Enrofloxacin</td>
<td>133 0 6 9 2 2 32</td>
<td>184</td>
</tr>
<tr>
<td>Folate pathway antagonist</td>
<td>Spectinomycin</td>
<td>3 0 38 115 4 24</td>
<td>184</td>
</tr>
<tr>
<td>Folate pathway antagonist</td>
<td>Trimethoprim/sulfa methoxazole</td>
<td>179 0 5</td>
<td>184</td>
</tr>
<tr>
<td>Lincosamide</td>
<td>Clindamycin</td>
<td>2 0 0 0 0 10 96 44 32</td>
<td>184</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Ceftiofur</td>
<td>177 0 3 2 0 1 1 0</td>
<td>184</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Gamithromycin</td>
<td>14 0 1 0 1 0</td>
<td>16</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Tildipirosin</td>
<td>9 0 5 0 0 1</td>
<td>15</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Tilmicosin</td>
<td>86 9 37 15 3 3 31</td>
<td>184</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Tulathromycin</td>
<td>3 0 18 81 29 5 7 3 24</td>
<td>170</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Tylosin tartrate</td>
<td>2 0 0 0 0 2 60 120</td>
<td>184</td>
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<tr>
<td>Penicillins</td>
<td>Ampicillin</td>
<td>146 0 9 3 1 1 2 7 15</td>
<td>184</td>
</tr>
<tr>
<td>Penicillins</td>
<td>Penicillin</td>
<td>77 0 50 17 12 0 3 4 21</td>
<td>184</td>
</tr>
<tr>
<td>Phenicol</td>
<td>Florfenicol</td>
<td>3 0 92 57 7 2 1 22</td>
<td>184</td>
</tr>
<tr>
<td>Pleuromutilin</td>
<td>Tiamulin</td>
<td>1 0 0 3 54 103 19 4</td>
<td>184</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Chlortetracycline</td>
<td>57 0 53 12 15 15 17</td>
<td>169</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Oxytetracycline</td>
<td>85 0 20 4 1 9 46</td>
<td>165</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Tetracycline</td>
<td>10 0 2 0 2 1 0</td>
<td>15</td>
</tr>
</tbody>
</table>
Cattle – *Mannheimia haemolytica* - % sensitive

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>% Sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>79.3%</td>
</tr>
<tr>
<td>Ceftiofur</td>
<td>98.9%</td>
</tr>
<tr>
<td>Danofloxacin</td>
<td>74.3%</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>75.5%</td>
</tr>
<tr>
<td>Gamithromycin</td>
<td>93.8%</td>
</tr>
<tr>
<td>Penicillin</td>
<td>69.0%</td>
</tr>
<tr>
<td>Spectinomycin</td>
<td>84.8%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>80.0%</td>
</tr>
<tr>
<td>Tildipirosin</td>
<td>93.3%</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>71.7%</td>
</tr>
<tr>
<td>Tulathromycin</td>
<td>80.0%</td>
</tr>
</tbody>
</table>

Data from < 20 isolates
Companion animal AST reporting – *E. coli*

- *E. coli*
- **Dog, cat**
  - Separate UTIs from remaining isolates
  - **UTIs**
  - **Other**
**Dog E. coli – skin, soft tissue, wound**

| MIC value | <=0.12 | 0.12 | <=0.25 | 0.25 | <=0.5 | 0.5 | <=1 | 1 | <=2 | 2 | >2 | <=4 | 4 | >4 | <=8 | 8 | >8 | <=16 | 16 | >16 | <=32 | 32 | >32 | <=64 | 64 | Total Isolates |
|-----------|--------|------|--------|------|-------|-----|-----|----|------|---|----|-----|---|----|-------|---|-----|-------|---|-----|-------|---|-------|
| 1st gen cephalosporin | Cefazolin* | 27 | 0 | 50 | 8 | 4 | 0 | 0 | 25 | 114 |
| 1st gen cephalosporin | Cephalexin* | 0 | 0 | 0 | 0 | 37 | 49 | 3 | 25 | 114 |
| 3rd gen cephalosporin | Cefovecin | 9 | 0 | 45 | 32 | 3 | 1 | 0 | 24 | 114 |
| 3rd gen cephalosporin | Cefpodoxime | 88 | 0 | 0 | 1 | 0 | 25 | 114 |
| 3rd gen cephalosporin | Ceftazidime | 96 | 0 | 4 | 8 | 6 | 114 |
| aminoglycoside | Amikacin | 107 | 0 | 6 | 0 | 0 | 0 | 0 | 113 |
| aminoglycoside | Gentamicin | 3 | 0 | 65 | 29 | 4 | 1 | 1 | 11 | 114 |
| B lactam combo | Amoxicillin/Clavulanic acid* | 0 | 0 | 0 | 2 | 10 | 64 | 15 | 23 | 114 |
| B lactam combo | Piperacillin/tazobactam | 0 | 0 | 0 | 2 | 10 | 64 | 15 | 23 | 114 |
| fluoroquinolone | Enrofloxacin | 88 | 0 | 3 | 3 | 2 | 1 | 0 | 17 | 114 |
| fluoroquinolone | Marbofloxacin | 88 | 0 | 3 | 3 | 2 | 1 | 0 | 17 | 114 |
| fluoroquinolone | Orbifloxacin | 92 | 0 | 4 | 1 | 0 | 0 | 0 | 17 | 114 |
| fluoroquinolone | Pradofloxacin | 95 | 0 | 2 | 0 | 1 | 16 | 114 |
| folate pathway inhibitors | Trimethoprim/sulfamethoxazole | 99 | 0 | 2 | 0 | 1 | 12 | 114 |
| penems | Imipenem | 0 | 0 | 0 | 0 | 0 | 0 | 114 |
| penicillins | Ampicillin* | 5 | 0 | 33 | 60 | 7 | 2 | 7 | 114 |
| phenicol | Chloramphenicol | 0 | 0 | 6 | 37 | 39 | 9 | 6 | 17 | 114 |
| tetracyclines | Doxycycline | 88 | 0 | 2 | 0 | 24 | 114 |
| tetracyclines | Tetracycline | 88 | 0 | 2 | 0 | 24 | 114 |

**Antibiotics with separate breakpoints for dog E. coli UTIs.**

ESBL testing is indicated for isolates with cefpodoxime MIC >= 8 ug/ml, or >2 ug/ml for ceftazidime.
# Dog E. coli – UTI

| MIC value | Antibiotic          | <=0.06 | <=0.12 | <=0.25 | 0.25 | <=0.5 | 1.0 | <=1 | 1.5 | >2 | <=4 | 4.0 | >4 | <=8 | 8.0 | >8 | 16 | >16 | >20 | <=32 | >32 | >64 | Total Isolates |
|-----------|---------------------|--------|--------|--------|------|-------|-----|-----|-----|----|-----|-----|----|-----|-----|----|-----|-----|------|-----|-----|----------------|
|           | Amikacin            | 157    | 0      | 6      | 0    | 0     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 163             |
|           | Amoxicillin/Clavulanic acid | 0     | 0      | 6      | 0    | 0     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Ampicillin          | 0      | 2      | 10    | 3    | 2     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Cefazolin           | 38     | 0      | 57    | 10   | 3     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Cefovecin           | 6      | 61     | 0     | 2    |       |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Cefpodoxime         | 131    | 143    | 0     | 6    |       |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Ceftazidime         | 38     | 0      | 61    | 10   | 3     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Cephalexin          | 0      | 0      | 0     | 1    | 1     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Chloramphenicol     | 1      | 0      | 1     | 32   | 103   | 20  | 2   | 6   |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Doxycycline         | 1      | 0      | 2     | 41   | 75    | 22  | 5   | 18  |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Enrofloxacin        | 137    | 0      | 4     | 4    | 2     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Gentamicin          | 11     | 1      | 87    | 53   | 2     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Imipenem            | 163    | 0      | 0     | 1    | 0     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Marbofloxacin       | 139    | 0      | 2     | 5    | 1     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Orifloxacina        | 141    | 0      | 5     | 1    |       |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Piperacillin/ tazobactam | 158    | 0      | 4     | 0    | 1     |     |     |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Pradofloxacin       | 145    | 0      | 2     | 0    | 2     | 15  |    |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Tetracycline        | 141    | 0      | 1     | 1    | 21    |     |    |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
|           | Trimethoprim/ sulfamethoxazole | 137    | 0      | 4     | 2    | 2     | 19  |    |     |    |     |     |    |     |     |    |     |     |      |     |     | 164             |
Companion animal AST reporting – *S. intermedius* group

Staph. intermedius group

- Separate UTIs from remaining isolates
  - UTIs
  - Other

- Separate OX-S* from OX-R*
  - UTI-OX-S
  - UTI-OX-R
  - UTI-OX-S
  - UTI-OX-R

* Oxacillin sensitivity/resistance based on human breakpoints
Proposed Changes-Y2

Isolates surveyed:
- Drop *Salmonella* except cattle
- Add *Strep. suis* for swine
- Add *Pasteurella multocida* for poultry
- Add *Step. equi/zooepidemicus* for horses

Increase maximum number of isolates for some categories

Increase reimbursement pricing

Improve reporting process, move all labs to spreadsheet uploader

Whole genome sequencing of selected isolates

<table>
<thead>
<tr>
<th>Bacterial pathogen + animal species</th>
<th>Target no. of isolates/year per laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mannheimia haemolytica - cattle</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Escherichia coli - cattle</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Escherichia coli – swine</em></td>
<td>40</td>
</tr>
<tr>
<td><em>Escherichia coli – poultry</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Escherichia coli – horses</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Escherichia coli – dogs</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Escherichia coli – cats</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Salmonella enterica - cattle</em></td>
<td>65*</td>
</tr>
<tr>
<td><em>Streptococcus suis – swine</em></td>
<td>40</td>
</tr>
<tr>
<td><em>Pasteurella multocida – poultry</em></td>
<td>40</td>
</tr>
<tr>
<td><em>Streptococcus equi or S. zooepidemicus – horses</em></td>
<td>40</td>
</tr>
<tr>
<td><em>Staphylococcus intermedius group</em>* - dogs*</td>
<td>65*</td>
</tr>
<tr>
<td><em>Staphylococcus intermedius group</em>* - cats*</td>
<td>40</td>
</tr>
</tbody>
</table>
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