

# Opportunities for Laboratory Testing to Inform Antimicrobial Use for Bovine Respiratory Disease: Application of Information Quality Value Stream Maps in Commercial Feedlots

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## Supplementary Tables

Supplementary tables include detailed descriptions of the Kaizen identified for each lane of the information quality value stream map (IQ-VSM) (Table 4) along with the information quality dimensions for each:

- **Granularity:** the degree of resolution for which the considered information is available
- **Frequency:** the time interval in which the information is acquired or has been updated
- **Accuracy:** the degree to which the obtained information represents the real-life phenomenon

The cell shading colours used on each of the tables are matched to the corresponding items on the IQ-VSM (Figure 2, Supplementary Figure S3).

**Supplementary Table S1.** The information quality matrix for the Kaizen (opportunities for continuous improvement) identified for the Process Lane of the future state Information Quality Value Stream Map (IQ-VSM) (Figure 2, Supplementary Figure S3) of Bovine Respiratory Disease (BRD) treatment plans used in a western Canadian commercial beef cattle feedlot production system.

Process Lane Kaizen: production processes	Granularity	Frequency	Accuracy
<p><b>KAIZEN 1</b></p> <p><b>ON-ARRIVAL PROCESS</b></p> <p>The ‘on-arrival’ process provides the 1<sup>st</sup> continuous improvement (Kaizen) opportunity for collection of deep nasal pharyngeal samples (DNPS) for laboratory testing (metagenomic or culture/AST data).</p> <p>DNPS could be collected from a representative sample of calves from a sample of purchase lots designated as high risk (HR) for BRD, <u>prior to antimicrobial metaphylaxis, sorting, &amp; pen assignment</u>. At this sample time point, there would have been <b>fewer opportunities for</b></p>	<p>The factor that most directly influences <b>granularity of sample collection</b> is <b>sample size</b>.</p> <p>The veterinarian would determine (i) <b>how many calves within each HR purchase lot</b> would be sampled* and (ii) <b>how many HR purchase lots within the current run</b> are to be sampled*.</p> <p>The veterinarian could also <b>consider how both the cost and time required</b> to collect the DNPS <b>affects the sample size decision</b>.</p> <p>Note: laboratory test results will follow in the Information Lane.</p> <p><i>*Research will inform veterinary decisions on the level of certainty</i></p>	<p>Numerous purchase lots continuously arrive at the feedlot throughout the ‘fall run’; however, only <b>a portion of HR purchase lots would be sampled at the time of ‘on-arrival’ processing</b> (sample time point 1).</p> <p>The veterinarian would determine <b>the sampling rate</b> and other criteria needed to select <b>which HR purchase lots will be sampled</b>. For example, a veterinarian might sample every 5<sup>th</sup> or every 10<sup>th</sup> HR purchase lot as they arrive and are processed at the feedlot.</p>	<p>As sample size influences granularity, <b>changing sample size influences the accuracy of what is measured</b> in the samples collected ‘on-arrival’ (sample time point 1).</p> <p>The veterinarian would determine an <b>appropriate sample size to reflect the anticipated purchase lot-level prevalence of AMR for specific BRD pathogens</b> present in the respiratory samples.</p> <p>In addition, having the <b>DNPS sampling process carried out by trained veterinary professionals</b> (registered veterinary technologists or veterinarians) <b>following a standard operating procedure (SOP)</b> to collect, label, and ship the temperature-controlled samples within 24 hours of collection would <b>increase the accuracy of what is</b></p>

Process Lane Kaizen: production processes	Granularity	Frequency	Accuracy
contagious BRD pathogens to spread & infect purchase lot mates.	<i>expected with different sample sizes.</i>		<b>measured</b> in the ‘on-arrival’ samples.
<p><b>KAIZEN 2</b></p> <p><b>PEN SAMPLING</b></p> <p>The ‘<b>pen sampling</b>’ process provides a 2<sup>nd</sup> continuous improvement (<b>Kaizen</b>) <b>opportunity</b> for collection of DNPS for <b>laboratory testing</b> (metagenomic or culture/AST data).</p> <p>DNPS could be collected from a <b>representative sample of calves</b> from a <b>sample of pens</b> designated as HR for BRD, <b>≈ 10 to 14 days after antimicrobial metaphylaxis, sorting, &amp; pen assignment</b>. By this time, there have been <b>many opportunities for contagious BRD pathogens to infect pen mates</b>. This</p>	<p>The factor that most directly influences <b>granularity of sample collection</b> is <b>sample size</b>.</p> <p>The veterinarian would determine <b>(i) how many calves within each HR pen</b> are to be sampled* and <b>(ii) how many HR pens within the current run</b> are to be sampled*.</p> <p>The veterinarian could also <b>consider how both the cost and time required</b> to collect the DNPS <b>affects the sample size decision</b>.</p> <p>Note: laboratory test results will follow in the Information Lane.</p> <p><i>*Research will inform veterinary decisions on the level of certainty</i></p>	<p>Numerous HR pens are established throughout the ‘fall run’; only a portion of HR pens would be sampled <b>shortly after arrival for ‘pen sampling’</b> (sample time point 2).</p> <p>The veterinarian would determine the <b>feasibility of sample collection at this sample time point</b>, based on availability of labor and processing facilities.</p> <p>The veterinarian would then determine the <b>appropriate timing of sample collection relative to feedlot arrival, the post-metaphylactic interval, and anticipated peak of BRD cases</b>.</p> <p>Lastly, the veterinarian would determine <b>the pen-level</b></p>	<p>As sample size influences granularity, <b>changing sample size influences the accuracy of what is measured</b> in the samples collected at ‘pen sampling’ (sample time point 2).</p> <p>The veterinarian would determine an <b>appropriate sample size and timing of sampling collection to reflect the anticipated pen-level prevalence of AMR for specific BRD pathogens</b> present in the respiratory samples.</p> <p>In addition, having the <b>DNPS sampling process carried out by trained veterinary professionals</b> (registered veterinary technologists or veterinarians) <b>following a standard operating procedure (SOP)</b> to collect, label and ship the cooled samples within 24 hours of collection would <b>increase the</b></p>

Process Lane Kaizen: production processes	Granularity	Frequency	Accuracy
sampling should <b>occur before the anticipated peak of 1st treatment for BRD</b> for the sampled pen.	<i>expected with different sample sizes.</i>	<b>sampling rate</b> to select <b>which HR pens will be sampled</b> . For example, a veterinarian might select and sample every 5 <sup>th</sup> or every 10 <sup>th</sup> HR pen as they are established at the feedlot.	<b>accuracy of what is measured</b> in the samples collected at 'pen sampling'.

Process Lane Kaizen: production processes	Granularity	Frequency	Accuracy
<p><b>KAIZEN 3</b></p> <p><b>IDENTIFY &amp; MANAGE PEN OUTBREAK</b></p> <p>The <b>process to ‘identify &amp; manage a pen outbreak’</b> provides a <b>3rd</b> continuous improvement (<b>Kaizen</b>) <b>opportunity</b> for collection of DNPS for <b>laboratory testing</b> (metagenomic or culture/AST data) <u>if the outbreak pen is treated with injectable antimicrobials or re-vaccinated.</u></p> <p><b>DNPS could be collected from a representative sample of cattle from outbreak pens</b> as they are processed through the hospital facility for <b>fever assessment, BRD treatment, or re-vaccination.</b></p>	<p>The factor that most directly influences <b>granularity of sample collection</b> is <b>sample size</b>.</p> <p>The veterinarian would determine <b>how many cattle within each outbreak pen</b> are to be sampled*.</p> <p>The veterinarian could also <b>consider how both the cost and time required</b> to collect the DNPS <b>affects the sample size decision.</b></p> <p>Note: laboratory test results will follow in the Information Lane.</p> <p><i>*Research will inform veterinary decisions on the level of certainty expected with different sample sizes.</i></p>	<p>As this <b>third opportunity for DNPS sample collection</b> occurs sporadically, the veterinarian could collect DNPS for <b>laboratory testing from as many outbreak pens as feasible as cattle are processed through the hospital facility</b> for fever assessment, BRD treatment, or re-vaccination (sample time point 3).</p>	<p>As sample size influences granularity, <b>changing sample size influences the accuracy of what is measured</b> in the ‘pen outbreak’ samples, collected at sample time point 3.</p> <p>The veterinarian would determine an <b>appropriate sample size to reflect the anticipated ‘outbreak’ pen-level prevalence of AMR for specific BRD pathogens</b> present in the respiratory samples.</p> <p>In addition, having the <b>DNPS sampling process carried out by trained veterinary professionals</b> (registered veterinary technologists or veterinarians) <b>following a standard operating procedure (SOP)</b> to collect, label and ship the cooled samples within 24 hours of collection would <b>increase the accuracy</b> of what is measured in the ‘pen outbreak’ samples.</p>

**Supplementary Table S2.** The information quality matrix for the Kaizen (opportunities for continuous improvement) identified for the Information Lane of the future state IQ-VSM (Figure 2, Supplementary Figure S3) of BRD treatment plans used in a western Canadian commercial beef cattle feedlot production system.

Information Lane Kaizen: BRD information processes	Granularity	Frequency	Accuracy
<p><b>KAIZEN 1</b></p> <p><b>INDIVIDUAL CALF LABORATORY, BRD TREATMENT, AND MORTALITY RECORDS</b></p> <p>Individual calf laboratory, BRD treatment, and mortality records contribute to an information process that was identified as Kaizen, as laboratory test results (metagenomic or culture/AST data) could be <u>uploaded at the individual calf level</u>.</p> <p>Note: in the proposed future state VSM, laboratory results would not be used to inform individual calf-level BRD treatment decisions.</p>	<p><b>ARGs/mutations or phenotypic AMR for specific BRD pathogens</b> would be reported by the laboratory. <b>Individual calf laboratory test results</b> could be <b>uploaded</b> into the feedlot management software and <b>outcomes reported</b> for each of the available sampling time points: 1, 2 or 3.</p> <p><b>A potential strength of long-read metagenomics compared to culture/AST data is the degree of resolution.</b> Long-read metagenomics has the potential to assess (in a single sample) AMR in (i) more types of bacteria, (ii) more types of genes and mutations, from (iii) more classes of antimicrobials than AST.</p> <p><b>The granularity of culture/AST data is influenced by:</b> (i) the</p>	<p>As sampling protocols, shipping time, laboratory processing time, laboratory reporting time and information communications technologies improve, the time interval from sample collection to acquired laboratory results will decrease.</p> <p><b>Uploading of laboratory results for each sampled calf</b> into the feedlot management software <b>could occur as the laboratory results become available.</b></p> <p><b>The laboratory test results in each individual calf record would be reported with the time the sample was collected:</b> (i) on-arrival (sample time point 1), (ii) pen sampling (sample time point 2), or (iii) management of pen outbreak (sample time point 3).</p>	<p><b>Accuracy</b> of laboratory results from each sampling time point <b>would be influenced by sample-level diagnostic sensitivity (Se) &amp; specificity (Sp)</b> for detection of ARGs/mutations or phenotypic AMR for specific BRD pathogens.</p> <p><b>The Se &amp; Sp of long read metagenomics would be influenced by:</b></p> <p>(i) enrichment, DNA extraction &amp; quality, host depletion, library preparation, (ii) flow cell performance, (iii) bioinformatics for pathogen &amp; ARG detection (databases(s) &amp; tool(s)), (v) whether AMR is encoded by genes or single point mutations, &amp; (vi) the extent to which ARG detection predicts AMR phenotype.</p> <p><b>The Se &amp; Sp of culture/AST are influenced by:</b> (i) sample quality &amp;</p>

Information Lane Kaizen: BRD information processes	Granularity	Frequency	Accuracy
	number of species and isolates tested for susceptibility, as well as the (ii) antimicrobials tested and the (iii) range of antimicrobial concentrations included in a laboratory test panel.		shipping time, (ii) the culture & species detection methods used, and (iii) the availability of evidence-based minimum inhibitory concentration (MIC) breakpoints for phenotypic interpretation.
<p><b>KAIZEN 2</b></p> <p><b>PEN-LEVEL SUMMARY OF INDIVIDUAL LABORATORY, BRD TREATMENT, AND MORTALITY RECORDS</b></p> <p>Pen-level laboratory, BRD treatment, and mortality summary is an information process that was <b>identified as Kaizen</b>, as uploaded laboratory test results (metagenomics or culture/AST data) could be <u>summarized at the pen-level</u>.</p>	<p>Within the feedlot management software, (i) <b>individual calf laboratory test results</b> could be <b>compiled and summarized for each pen</b>, and (ii) the <b>95% confidence intervals (CIs) for the prevalence of reported laboratory outcomes</b> (ARGs/mutations or phenotypic AMR for specific BRD pathogens) could be <b>calculated</b>. <b>Outcomes could then be reported</b> for each of the available sample times: 1, 2 or 3.</p> <p>The <b>95% CIs</b> would vary based on the <b>number of samples with data per pen</b>.</p> <p><b>Summarized pen-level laboratory results</b> would be</p>	<p><b>As the pen-specific individual calf laboratory results become available</b> from each sampling time point, the feedlot management software could <b>automatically update the pen summary</b>. This <b>pen summary of the laboratory testing data with 95% CIs</b> for each sampled pen <b>would be available as data are received and uploaded in the feedlot software</b>. The <b>summarized laboratory results in each pen report would be reported with the time the sample was collected</b>: (i) on-arrival, (ii) pen sampling, or (iii) management of pen outbreak.</p> <p><b>Summarized pen-level laboratory results</b> could be</p>	<p><b>Accuracy of the results</b> for each specific sampling time point <b>would be influenced by pen-level Se and Sp</b> for detection of ARGs/mutations or phenotypic AMR by BRD pathogen.</p> <p><b>Pen-level Se &amp; Sp</b> would be influenced by: (i) <b>diagnostic Se &amp; Sp of the assay for the individual samples</b>, (ii) <b>sample size at the pen level</b> (granularity), and the (iii) <b>user-defined pen-level AMR threshold</b> (prevalence or number of AMR positives).</p> <p><b>BRD pathogens are contagious</b>, spread between calves through nose-to-nose contact and respiratory aerosols. The <b>influence of sample size on accuracy of assessing pen</b></p>

Information Lane Kaizen: BRD information processes	Granularity	Frequency	Accuracy
Note: this pen-level summary of laboratory data could then be used in the Information Processing Lane to assess antimicrobial treatment strategies for BRD.	<p><b>compared against the pen-level user-defined AMR threshold.</b></p> <p>If the <b>user-defined AMR threshold is exceeded</b>, this information will be <b>flagged</b> in the pen summary and a <b>pen-specific alert notification will be</b> sent to the <b>veterinarian</b>.</p>	<p><b>automatically compared against the pen-level user-defined AMR threshold. If this AMR threshold were exceeded at any of the sampling time points,</b> this information could <u><b>automatically trigger</b></u> a <b>pen-specific alert notification</b> to be sent to the <b>veterinarian</b>.</p>	<p><b>AMR status will depend on the timing of sample collection relative to opportunities for transmission of BRD pathogens</b> among calves within a pen. <b>Pen-level prevalence of known BRD pathogens changes significantly throughout the early feeding period (24,27).</b></p>



Information Lane Kaizen: BRD information processes	Granularity	Frequency	Accuracy
<p><b>KAIZEN 3</b></p> <p><b>FEEDLOT-LEVEL SUMMARY OF PEN-LEVEL LABORATORY, BRD TREATMENT, AND MORTALITY RECORDS</b></p> <p>Feedlot-level laboratory, BRD treatment, and mortality summary is an information process that was identified as Kaizen as pen-level laboratory test results (metagenomics or culture/AST data) could be <u>summarized at the feedlot-level</u>.</p> <p>Note: this feedlot-level summary of laboratory data could then be used in the Information Processing Lane to assess antimicrobial treatment strategies for BRD.</p>	<p>Within the feedlot management software, (i) the <b>number and proportion of HR pens and/or outbreak pens sampled</b>, (ii) and the <b>prevalence of reported laboratory outcomes</b> (ARGs/mutations or phenotypic AMR for specific BRD pathogens) <b>with 95% CIs from each sampled pen</b> could be be <b>compiled and summarized</b>. Feedlot-level summaries would be reported <b>with 95% CIs adjusted for clustering by pen</b> for each available sample time: 1, 2 or 3.</p> <p>This feedlot-level report would illustrate the <b>central tendency and uncertainty in the prevalence of ARGs/mutations or phenotypic AMR for specific BRD pathogens across sampled HR pens and/or outbreak pens</b> for each sample time.</p> <p>The <b>number &amp; identity of sampled pens where the user-defined AMR threshold had been</b></p>	<p><b>As laboratory results are uploaded</b>, the feedlot management software could <b>automatically update the sampled pen summary</b> for each sample time (1, 2 or 3) and then <b>automatically update the feedlot summary for all sampled pens within the feedlot</b>. The summarized laboratory results in the feedlot report would be reported for <b>each sample time points</b>: (i) on-arrival, (ii) pen sampling, or (iii) management of pen outbreak.</p> <p>This feedlot summary of laboratory results with 95% CIs adjusted for clustering by pen would be available as data are received and uploaded to the feedlot management software.</p> <p>The <b>number and identity of sampled pens where the user-defined AMR threshold had been exceeded (triggered pens)</b></p>	<p><b>Accuracy of the results for each specific sampling time point</b> would be influenced by <b>feedlot-level Se and Sp</b> for detection of ARGs or phenotypic AMR by BRD pathogen.</p> <p>Feedlot level Se and Sp would be influenced by (i) the <b>individual sample diagnostic Se and Sp</b>, (ii) the <b>sample size at the pen level</b> (granularity), (iii) the <b>user defined pen-level AMR threshold</b> (prevalence or number of AMR positives), (iv) the <b>number of pens sampled</b>, (v) <b>central tendency and uncertainty in the prevalence of ARGs/mutations or phenotypic AMR for specific BRD pathogens across sampled HR pens</b>, and (vi) the <b>number of sampled pens that exceed the user-defined AMR threshold</b>.</p>

Information Lane Kaizen: BRD information processes	Granularity	Frequency	Accuracy
	exceeded (triggered pens) would be reported.	would automatically be updated.	

**Supplementary Table S3.** The information quality matrix for the Kaizen (opportunities for continuous improvement) identified for the Information Processing Lane of the future state IQ-VSM (Figure 2, Supplementary Figure S3) of BRD treatment plans used in a western Canadian commercial beef cattle feedlot production system.

Information Processing Lane Kaizen: BRD information assessment and processing	Granularity	Frequency	Accuracy
<p><b>KAIZEN 1</b></p> <p><b>BASED ON PEN-LEVEL LABORATORY RESULTS, WAS THE USER-DEFINED PEN-LEVEL AMR THRESHOLD EXCEEDED?</b></p> <p>This <b>information processing step</b> was identified as <b>Kaizen</b> as it provided an <b>opportunity to use the summarized pen-level laboratory test results (metagenomics or culture/AST data)</b> from each <b>triggered pen as part of the veterinarian's decision-making process</b></p>	<p>As previously mentioned in the information lane, <b>if the user-defined pen-level AMR threshold had been exceeded at any of the sampling time points</b> in the current run, this information would <b>trigger</b> the feedlot management software to send a <b>pen-specific alert notification to the veterinarian.</b></p> <p>The <b>veterinarian</b> would review the <b>summarized laboratory results for the 'triggered pen', and determine if (i) the number of calves sampled, and (ii) the 95% CIs on the prevalence of reported laboratory outcomes (ARGs/mutations or phenotypic AMR for specific BRD pathogens) provide sufficient information to question the</b></p>	<p><b>To be most effective, pen specific laboratory test results for sample time point 1 and/or sample time point 2 would be uploaded, summarized, and analyzed for the veterinarian to review prior to peak incidence for first treatment for BRD.</b> Typically, the veterinarian would be reviewing results for specific pens when alerted by the feedlot management software.</p> <p>The <b>veterinarian could utilize the pen-level laboratory test results to inform decisions on the appropriateness of current BRD treatment protocols</b> for the (i) <b>sampled HR pen, and +/- (ii) other similar but non-sampled HR pens</b> during the current run.</p>	<p>The <b>accuracy</b> of decisions to adapt a treatment protocol for a specific 'triggered pen' would depend on the strength of the association between detected ARGs/mutations or AMR phenotype for specific BRD pathogens and response to BRD treatment.</p> <p>The accuracy of any resulting decisions would also depend on the appropriateness of the pen-level, user-defined AMR threshold for informing expected treatment success and expectations for responsible AMU. Components that could influence the decision to adapt the treatment protocol for a pen might include: (i) by how much was the threshold exceeded? (ii) which BRD pathogen(s) were detected? (iii) which ARGs were</p>

Information Processing Lane Kaizen: BRD information assessment and processing	Granularity	Frequency	Accuracy
regarding the <b>appropriateness of the current BRD treatment protocol</b> for each <b>triggered pen</b> .	<b>appropriateness of the current BRD treatment protocol for the 'triggered pen'</b> and potentially for <b>other similar but non- sampled neighboring pens</b> during the current run.	<b>Pen-specific laboratory test results</b> for <b>sample time point 3 (pen BRD outbreaks)</b> would be <b>uploaded, summarized, and analyzed for the veterinarian to review</b> in the event that similar non-sampled neighboring pens experience an outbreak of BRD.	detected? (iv) which sampling time point were data from? (v) what is the positive predictive value of the tests at the pen-level for resistance to the drug/pathogen? (vi) what are the economics of the potential protocol change?

<p><b>KAIZEN 2</b></p> <p><b>DO CUMULATIVE FEEDLOT-LEVEL DATA ALIGN WITH CURRENT BRD TREATMENT DECISIONS?</b></p> <p>This <b>information processing step</b> was identified as a <b>Kaizen</b> as it provided an <b>opportunity to analyze and utilize the summarized feedlot-level laboratory results (metagenomics or culture/AST data) as part of the veterinarian's decision-making process about the appropriateness of the feedlot-level BRD treatment protocols in the current run and potentially for subsequent runs.</b></p>	<p>The veterinarian could evaluate <b>feedlot-level laboratory results, i.e., detection of ARGs/mutations or AMR phenotype for specific BRD pathogens from sampled HR and outbreak pens</b> using feedlot management software.</p> <p>The veterinarian could also consider the (i) <b>number of pens sampled</b>, (ii) <b>precision of AMR estimates at the pen level</b>, (iii) <b>number of triggered pens</b>, and (iv) <b>uncertainty of the AMR estimates at the feedlot-level</b> for subsequent decisions on <b>appropriateness of the current BRD treatment protocols at the feedlot-level, in addition to other information sources</b> such as (v) <b>acute and chronic BRD morbidity rates</b>, (vi) <b>BRD mortality rate</b>, (vii) <b>gross post mortem results</b>, and (viii) <b>other diagnostic data.</b></p>	<p>The <b><u>complete</u> AMR dataset for all sampled HR and outbreak pens</b> for each of sample times 1, 2 or 3 could be <b>automatically summarized</b> by the feedlot management software as <b>laboratory data become available.</b></p> <p>The <b><u>complete summarized</u> AMR dataset for all sampled HR and outbreak pens</b> should be available to the veterinarian in sufficient time to inform their decisions regarding the <b>appropriateness of the feedlot-level BRD treatment protocols for the current run and potentially for subsequent runs.</b></p>	<p><b>Currently the veterinarian considers the</b> (i) acute and chronic BRD morbidity rates, (ii) BRD mortality, (iii) gross post-mortem results, (iv) other diagnostic data and (v) economics of a potential BRD protocol change <b>when questioning the appropriateness of the current feedlot-level BRD treatment protocols.</b></p> <p>The veterinarian could also consider whether the <b><u>complete summarized</u> AMR dataset aligns with or suggests required changes to BRD treatment protocols in connection with the traditional morbidity and mortality dataset.</b></p> <p>The addition of AMR data from sampled HR and outbreak pens has the potential to <b>better inform the veterinarian when considering changes to BRD treatment protocols to achieve BRD treatment success</b> while considering antimicrobial stewardship goals for the industry.</p>
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## References

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