



Let's Connect

PP21: Novel Ways to Leverage Your Real-World Data Investment in Integrated Evidence

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ABSTRACT

Traditionally, Real World Data (RWD) has been used in health economics and outcomes research, market access evidence generation and post-marketing commitments. The FDA has released the final guidance, and these data can now serve multiple functions across the product value chain including integrated evidence package submissions.

This work covers novel applications of RWD to support activities such as clinical trial optimization, external control arms, integrated evidence package submissions, diversity plans and patient journey to determine unmet need, as well as applications in safety and pharmacovigilance and key considerations in their execution.

Leveraging RWD in accordance with the FDA RWE Guidance warrants new and advanced methods in machine learning, deep learning, artificial intelligence and simulation to manage data and generate the insights needed to execute these novel applications. We highlight key considerations in this work.

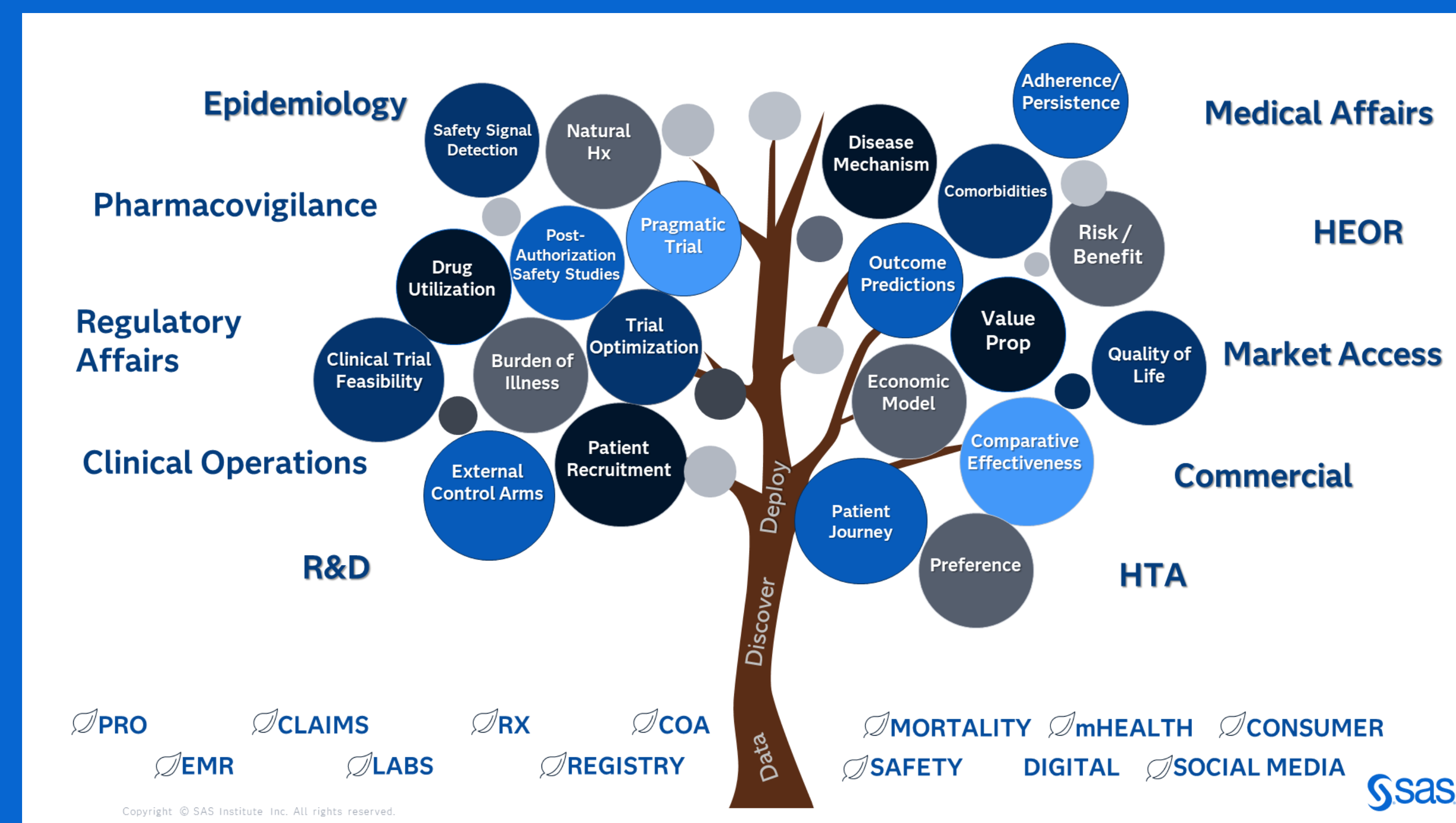


Figure 1. Developing Real World Evidence from Real World Data in Novel Ways Across the Product Value Chain

CLINICAL TRIAL OPTIMIZATION

GOAL: Define the optimal Target Patient Population (TPP) and simulate clinical trial enrollment

BENEFITS:

- Identify geographic distribution
- Reduce attrition and protocol amendments
- Simulate and monitor site performance

METHODS: Three TPP were defined using

1. Conventional means
 2. Subject matter expertise removal of exclusion criterion
 3. Machine learning (ML) analysis of variables of importance
- Variables of importance determined using Forest. Spatial analyses of geographic distribution. Univariate analyses of baseline characteristics.
 - Hypotheses tested to using multiple predictive and ML methods
 - Output was used as priors for simulation.

EXTERNAL CONTROL ARMS

GOAL: Provide sufficiently robust evidence with diverse sources of data to expedite regulatory approval.

BENEFITS:

- Shorten timelines
- Minimize patient burden and risk

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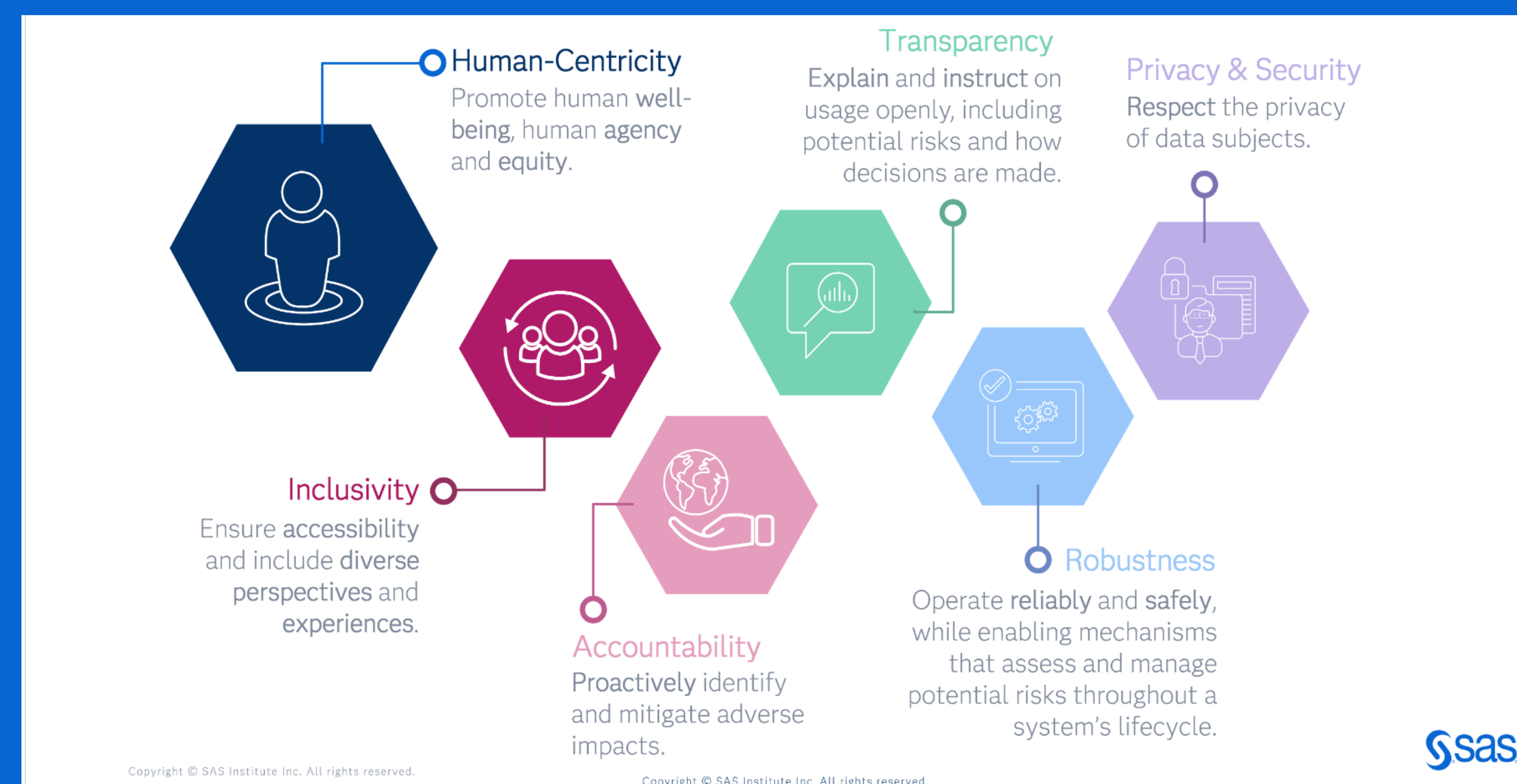


Figure 2. Principles of Responsible Innovation with ML/AI

DIVERSITY PLANS

GOAL: Have more representative and inclusive patient populations in clinical trials

BENEFITS: Establish a more inclusive and representative patient population.

METHODS:

- Assess bias in RWD compared to a true epidemiologic profile
- Simulate enrollment plans for each site
- Connect directly to Electronic Medical Records using interoperability adaptors (i.e. FHIR, OMOP, etc.)

CONCLUSION

- Use cases presented here and others in the figure demonstrate novel applications of RWD/RWE in the value chain of product development.
- Key considerations in submitting evidence using these data are critical to meet regulatory requirements and responsible drug development.
- Responsible ML and AI practices and procedures are every organization's responsibility as regulations continue to be developed.

KEY CONSIDERATIONS FOR RESPONSIBLE AND ETHICAL INTEGRATED EVIDENCE PACKAGES:

Technology

- Select the appropriate technology Implement industry standards
- Governance capabilities
- Model interoperability.
- Connect to and ingest big data and *a priori* standardize it before applying AI/ML techniques

Data Governance

- Data acquisition, integration, harmonization
- Assess data quality
- Track data lineage
- Version code

Model Operations

- Develop fit models
- Govern and monitor model performance
- Version models
- Establish a model operations process

Model Performance Bias

- Identify variable inputs
- Assess weight of each variable
- Detect any bias in the models
- Understand the source and collection of data used

Transparency

- Lineage of operations (data management and analyses)
- Explainability of models
- Understand any system limitations
- State assumptions in the data chain of custody
- Assess impact the projected and modeled outcomes of the trial

