ACRO Innovate Advocate Collaborate

ACRO's Principles for Responsible AI

ACRO is a trade association that represents clinical research organizations and technology companies that share a mission: advancing clinical research and enabling the delivery of new medicines to patients in need. ACRO member companies embrace AI technologies for their potential to accelerate medical advancements. At the same time, they recognize that potential harm can arise if these technologies are not developed and used responsibly.

ACRO believes that the following principles should guide the development and use of AI tools that may be deployed across the drug development life cycle:

1. **Conformance with Regulatory Expectations:** Organizations engaged in drug development activities should comply with applicable laws and regulations and review relevant guidance as those pertain to the development and use of AI tools.
2. **Ethical Considerations:** Organizations should take an approach to the development of AI technologies that aims to ensure that tools produce results that are equitable, fair, and free from unintended bias.
3. **Good Machine Learning Practices:** Organizations should follow good machine learning practices recommended by regulatory and other government and standards development bodies, such as NIST, in pursuing AI technologies that are relevant, safe and efficacious.
4. **Multi-disciplinary Teams and Senior Leadership Accountability:** Organizations should create multi-disciplinary teams to govern the development and deployment of AI technologies used in clinical development activities. They should designate a senior leader to be accountable for overseeing the effort.
5. **Quality in Design and Event Review:** ACRO recommends quality management processes include a specific focus on quality in the design of AI technologies as well as quality-related events arising in connection with AI technologies.
6. **Inventory Maintenance:** Organizations should maintain an up-to-date inventory of AI technologies they have deployed, including, as relevant, details of Foundational Models supporting these technologies.
7. **Responsible Data Usage:** When AI tools require training data, organizations should ensure that they have necessary permissions under relevant laws or regulations, including the assent or consent of individuals where required.
8. **Human Oversight:** Organizations in the life sciences will embrace the use of subject matter experts in the training and validation of AI models. Deployed AI technologies should be subject to human oversight including critical decision-making activities.
9. **Transparency in Use of AI:** At point of use, organizations should, to the extent possible, disclose the use and the manner of use of AI in drug development activities that may influence clinical data endpoints or patient safety.
10. **User Training and Guidance:** Organizations that develop and deploy AI tools used in drug development activities should provide training and guidance to users. In so doing, they should give careful consideration to user expertise and familiarity with AI tools in the intended setting.

The above principles describe an approach to “responsible AI” which emphasizes thoughtful design, transparency, and accountability in the context of drug development.

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ACRO's Guidelines for the Development of Responsible AI-Based Technology

The following guidelines, which are adapted from the work of the FDA, NIST, CDISC, ISPOR, and others, provide additional detail and locate the principles set out above within the clinical context of drug development.

1. **Multi-Disciplinary Expertise Is Leveraged Throughout the Total Product Life Cycle:**
   A diverse team ensures AI aligns with clinical goals, patient safety, and quality over the product's life cycle. This multidisciplinary approach ensures that clinical expertise, data quality, and machine learning proficiency are integrated at every stage of development.
   References: NIST Framework: "Prepare." NIST AI 100-1, CDISC, HL7, FHIR, and FAIR Data Principles; ISO/IEC 23053:2022(E) ISO Framework for Using Artificial Intelligence Systems Using Machine Learning.
2. **Good Software Engineering, Machine Learning, and Security Practices Are Implemented:**
   Sound software engineering, data quality, machine learning, and cybersecurity practices are implemented to protect sensitive patient data and ensure the reliability of software and AI model development.
   References: NIST Framework: "Protect." NIST AI 100-1, and FAIR Data Principles.
3. **Clinical Study Data Sets Are Representative of the Intended Population:**
   Organizations should ensure that the input dataset used for training is congruent with the desired output. For example, for patient datasets, organizations should ensure that the training dataset adequately represents the diversity of the intended patient population, thereby promoting unbiased and clinically relevant AI performance.
   References: NIST Framework: "Identify." NIST AI 100-1, and ISPOR guidelines for real-world data use.
4. **Independent Training and Testing:**
   Independence between training and testing data is maintained to detect and mitigate biases in AI models, ensuring their reliability and effectiveness. While complete avoidance of duplicate data being used both to train and test AI algorithms can be challenging to achieve in practice, careful selection and preparation of data is strongly recommended.
   References: NIST Framework: "Detect." NIST AI 100-1.
5. **Clinically Relevant Testing:**
   Rigorous testing is essential to generate clinically applicable insights into AI performance and ensure that deployed AI technologies are reliable in real-world clinical settings.
   References: NIST Framework: "Recover." NIST AI 100-1, and ISPOR guidelines.
6. **Model Design Is Tailored to the Available Data and Reflects the Intended Use of the Model:**
   Model design is tailored to clinical data, ensuring data security, patient safety, and alignment with clinical development requirements. It reflects the specific context of use for maximum relevance. In developing models, focus carefully on inputs (e.g., data selected for training) and outputs (performance). In selecting among competing models, the application of Occam's Razor (i.e., parsimony preferred) is generally a helpful rule of thumb.
   References: NIST Framework: "Recover." NIST AI 100-1.
7. **Focus Is Placed on the Performance of the Human-AI Team:**
   Human-in-the-loop AI reduces the potential for undesirable AI decision-making (e.g., based on hallucinations), and creates an expectation that the human operator is accountable for decision-making. In deploying AI models, developers should give careful consideration to the performance in

practice of the human overseeing the specific AI application (e.g., over longer passages of time-in-use).
References: NIST Framework: "Communicate." NIST AI 100-1.

8. **Data Rights and Transparent Information for Users:**
   Upholding data privacy and patient rights is paramount. GDPR, HIPAA, as well as other relevant data protection legislation and ethical AI Guidelines guide our practices. Users receive clear information about AI usage, data sources, limitations, and updates. Permission for data usage is ensured and incorporates required scientific review processes.
   References: NIST Framework: "Communicate." NIST AI 100-1, GDPR, HIPAA, and Ethical AI guidelines.
9. **Real-World Performance Monitoring:**
   Continuous monitoring helps maintain AI safety and effectiveness in real-world clinical use, ensuring that AI technologies adapt to changing clinical realities.
   References: NIST Framework: "Recover." NIST AI 100-1.
10. **Machine Retraining and Iterative Development:**
    Iterative model development addresses evolving clinical needs, ensuring sustained AI performance. However, it may also be essential to ensure the model does not drift over time towards a deteriorated performance level.
    References: Evolving Clinical Standards and best practices for iterative model development and retraining

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Appendix: Additional Framework References

1. **NIST Framework:** https://nvlpubs.nist.gov/nistpubs/ai/NIST.AI.100-1.pdf
2. **FAIR Data Principles**: These principles focus on making data Findable, Accessible, Interoperable, and Reusable. Ensuring data adheres to FAIR principles can enhance data quality, accessibility, and reusability in AI applications.
3. **Clinical Data Interchange Standards Consortium (CDISC)**: CDISC provides standards for the structure and format of clinical trial data. Integrating CDISC standards can improve the consistency and quality of data used for AI.
4. **HIPAA and GDPR Compliance**: Ensure that your AI systems comply with healthcare data privacy regulations like the Health Insurance Portability and Accountability Act (HIPAA) in the U.S. and the General Data Protection Regulation (GDPR) in Europe.
5. **Transparency Initiatives**: Leveraging transparency initiatives such as the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) can enhance the interpretability and reporting of AI models.
6. **Health Informatics Standards**: Explore standards like Health Level Seven (HL7) and Fast Healthcare Interoperability Resources (FHIR) for ensuring interoperability in healthcare data exchange.
7. **Real-World Evidence (RWE) Frameworks**: If you're using RWE for AI, consider frameworks like the Framework for FDA's Real-World Evidence Program for guidance on using real-world data effectively.
8. **Ethical AI Guidelines**: Integrate ethical AI guidelines such as those outlined in the Ethical AI Framework for Healthcare to ensure ethical considerations in AI development.
9. **Reproducibility and Replicability Standards**: Enhance principles related to model transparency by adopting the Reporting Guidelines for AI in Healthcare (RIGHT) and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) guidelines.