Beyond Metrics Through the Power of Artificial Intelligence:

Applications You Can Use in Quality Today

Inspiring collaboration. Leading innovation. Making a difference.



Join us and Imagine If...

Through the Xavier Artificial Intelligence Initiative

92 Members, including:







Team Role	Continuous Product Quality Assurance (CPQA)	How to Evaluate Continuously Learning Systems (CLS)
Team Leader	Charlene Banard Shire	Berkman Sahiner FDA
Team Leader	Dave Lonza Lachman	Mohammed Wahab Abbott
Team Administrator	Mark Zhong PwC	Mac McKeen Boston Scientific
Core Team Mentor	Tony Barnes Bucks County Advisors	Walt Mullikin Shire
Core Team AI Expert	Matt Schmucki AstraZeneca	Kumar Madurai CTG

FDA Interest in Al

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Message from the Commissioner





"AI holds enormous promise for the future of medicine," FDA Commissioner Scott Gottlieb said in prepared remarks to the Health Datapalooza conference in Washington, D.C.

The FDA is moving to encourage the use of artificial intelligence (AI) in health care, the agency's chief said Thursday. He said the FDA is working on an updated **"new regulatory framework"** that will allow regulators to keep up with new technology and "promote innovation in this space."

He said the FDA is working with experts to update the way it evaluates these new technologies in the approval process.

"Eventually, **AI tools could be integrated directly into smartphones or wearable devices** for a variety of early detection applications, reducing the need for expensive specialist visits while increasing the likelihood that we're catching potentially serious problems early. **These are no longer far-fetched ideas.**"

"This is it. This is the future of Quality."

Art Czabaniuk

FDA Pharmaceutical Program Director III, District Director, ORA

> "AI has the potential to fill in the gaps we cannot get to in our current approach/ paradigm."

Cisco Vicenty Program Manager, Case for Quality, CDRH

We are on this journey together!

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Al Explained

Getting Everyone on the Same Page

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Demystifying Al....





Artificial Intelligence: the broad based science of computers mimicking humans

Machine Learning: the method behind which machines learn from data

Deep Learning: a type of machine learning that is unsupervised through a deep neural network exchange of data





Machine Learning



Supervised

- Machine learns from training data
- You have input data and an output
- The machine learns how to map the input to the output



Unsupervised

- You have input data, but no output
- There is no correct answer and no teacher
- Algorithms must discover and present the interesting structure in the data



Reinforcement

- Trial and error method resembling how humans learn
- There is no answer key
- Agent rewarded when task is performed well e.g. video games, Pandora

CPQA: Continuous Product Quality Assurance

Exploring how AI can be used to predictively assure product quality



Imagine the power of:

Continuous Product Quality Assurance, instead of annual audits that assess <2% of your documents and information.

Today	AI Realized		
After the Fact	Predictive		
Periodic	Continuous		
Statistical Sample	Totality		

- Scan all of your documents constantly to identify trends you didn't even know existed.

Identify signals that predict impact to product quality.

What do Data Scientists Need?

Creation of a Data Lake

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Explore the Power of Al







Humans conduct analysis linearly to understand and solve problems...



Humans may follow multiple investigation routes but usually only one at a time, or one per team





Data Systems

Data Element	GxP Systems		Non-GxP Systems		
	LIMS	ERP	САРА	Patient Wearables	Weather
Country		x			X
Date of Manufacture	Х	x			X
Manufacturing Site		X	X		
Patient ID				X	
Product ID	Х	X	X	X	
Product Lot	Х	X	Х	x	
Sample Quantity	Х				
Region - Zone		x			x
Root Cause Code			Х		
Sample ID	X				
Sample Type	X				
Supplier ID					
Temperature					x

X = Data element resides in system

Data Elements

Need: Consistently structured data and shared data elements

Illustrative System Map



System

Data Element

Human

Analysis



CRM – Customer Relationship Management System

- CAPA Corrective Action and Preventive Action
- MES Manufacturing Execution System
- LIMS Lab Information Mgmt. System

- **ERP Enterprise Resource Planning System**
- FAR Field Action Report System
- CDMS Clinical Data Management System
- Dev. LIMS Development Lab Information Mgmt. System

Table Discussion





In what ways can Al be used in your organization?

CLS: Continuously Learning Systems

How to Evaluate a System that Continuously Learns

Problem Statement and Goal

Problem Statement:

- Deep learning systems continuously evolve
- How do we establish credibility and reliability of the outcomes?
- We can't use traditional validation methods

Goal:

- To maximize the advantages of AI for healthcare
- Identify how to provide confidence in the performance of continuously learning algorithms

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- Minimize risk to product quality and patient safety

System Architecture



Performance Evaluation

- Overall system test methods and tools
- Typically involves a comparison of what the CLS is supposed to do for a certain input versus what it actually does (i.e. Validation)

-Assistance Systems

- The CLS does not take action on its own
- Assists users in their decision making or for their actions (Augmented Intelligence)

-Autonomous Systems

• The CLS takes action or implements a decision without clinician or user intervention

System Architecture





SDLC Waterfall Model



As a continuous learning system the process architecture relies on the overlap and PDCA functionality to manage and maintain the performance of the algorithm





GmLP (Good Machine Learning Practices) similar to GxP outline criteria and considerations for developing best practices in AI/ML/CLS

- Introduction What does "good look like" for common applications in Med Device and Pharma solutions that incorporate CLS to have confidence in its safety and effectiveness through the TPLC
- Considerations for CLS associated with Performance Evaluation and building user confidence
 - Focus on how CLS development is different from traditional MedDev/Rx development
 - Covers the entire product lifecycle Planning through Retirement
 - Leverages lessons learned from other industries
- Flow Charts of logic and considerations to arrive at AI/CLS validation rules for certain applications in Med Device and Pharma
- Use Cases included in the paper as examples of how AI/CLS can be applied to life sciences
- Glossary of commonly used terms





FDA clearance in April 2018

- IDx-DR is <u>the first autonomous AI-based diagnostic system</u> for the autonomous detection of diabetic retinopathy, a leading cause of blindness
- IDx-DR <u>received expedited review under the FDA's Breakthrough Devices program</u> following a pivotal clinical trial conducted at 10 primary care sites across the U.S.
- Clinical study of 900 patients retinal images. IDx-DR identified mild diabetic retinopathy
 <u>correctly 87.4% of the time</u> and identified patients who did not have diabetic retinopathy
 <u>correctly 89.5% of the time</u>.



Clinically Relevant Algorithms developed with medical experts based on existing guidelines. Explainable

Deep learning searches the same signs of disease as a clinician, so we know how the AI came to its decision.



What would you need to know to feel confident in the output from a system that continuously learns?



Next Steps

Explainability – Choosing a New Doctor



Which Recommendation Would You Trust?



Explainability – Which one is Which????







Explainability – Link Input to Output



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CPQA:

- 1. Identify relevant non-GXP data to include in GMP decisions
- 2. Develop an algorithm to address a succinct business problem, and analyze publicly available data

Special Interest Groups:

- 1. Use of AI in Manufacturing Operations
- 2. Open Source AI applications in life sciences
- 3. Culture and infrastructure needed to implement AI successfully

Xavier 2018 Al Summit: August 23-24. www.XavierAl.com



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"But I Don't Think We Are Ready for Al"

Let me show you why you are, and how you can benefit right away



There is Something for Everyone

Crawl

Walk

Run

Is My Company Ready?



AI Working Team Output

- 1. Harmonize definitions of terms across systems
- 2. How to clean-up management of data.
- How to improve electronic searchability of data and access to the data.
- Identify interrelationships of data within and across systems, as well as across internal and external sources

How You Can Benefit Right Now

- You can use these suggestions for your company right away.
- 2. Important for your current operations.
- Critical to support current decisions being made regarding your product quality
- 4. This mapping of interrelationships can be used for human decisions right away.

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Xavier Al Summit. August 23-24, 2018 www.XavierAl.com

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