Designing the AI-Enabled CMC Ecosystem

For Drug Development and Manufacturing in a 10× Era

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* This presentation was produced by **the author**, augmented by **ChatGPT** tokens through **26** prompts and **4953** seconds of inference time (and **163** references).
** At Amgen, Pablo is a power user of **ChatGPT** Enterprise & MS **Copilot**.
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Perception vs Reality

Stochastic parrot

✓ **In-context learner** [1]
(approximating Bayesian updating)

Memorization oracle

✓ **Emergent reasoning** [2]
(language mastery and advanced reasoning patterns)

Search engine

✓ **Thought partner / Research assistant** [3]
(with tools; eg., "deep research")

Question-answer bot

✓ **Stepwise reasoning** [4]
(prompt scaffolding / chain-of-thought)

Text-only inputs

✓ **Multi-modal reasoning**
(text + images + data)

Uncontrollable hallucinations

✓ **Grounded, verifiable responses** [5]
context + retrieval (RAG) to reduce hallucinations

1) https://arxiv.org/pdf/2402.03175; 2) https://arxiv.org/pdf/2501.12948; 3) https://arxiv.org/pdf/2506.12594
4) https://arxiv.org/pdf/2201.11903; 5) https://arxiv.org/pdf/2005.11401

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Guiding Principles

Lens for Case Studies

Good AI practice in drug development

1) Human-centric by design

Use aligns with ethical and human-centric values.

2) Risk-based approach

Validation and controls are proportional to risk, based on context of use.

3) Adherence to standards

Adhere to all relevant standards, including technical, scientific, and regulatory.

4) Clear context of use

Have a well-defined context of use.

5) Multidisciplinary expertise

Integrate multidisciplinary expertise across the life cycle.

6) Data governance & documentation

Ensure data provenance, traceability, privacy, and documentation.

7) Model design & development practices

Use fit-for-purpose data and best practices to promote "trustworthiness".

8) Risk-based performance assessment

Performance evaluation of the complete (human-AI) system is proportional to risk.

9) Life cycle management

Adopt risk-based quality management across the life cycle.

10) Clear, essential information

Communicate to the intended audience all relevant information in plain language.

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AI4x Suite – Grounded Knowledge Work at Scale

AI4x Suite: consists of multiple LLM-based systems that tap into >2.0m controlled documents and >1.5m curated experiments in the Amgen's corporate knowledge base.

AI solution characteristics	FDA principles anchored
RAG[1] grounded responses → reduced hallucinations, full traceability… (hyperlinks to references).	7) *Model design & development practices* → "promotes transparency, reliability, (…) and robustness"
Not a "vanilla" ChatGPT → multimodal reasoning, agents, and various optimizations increase accuracy.	5) *Multidisciplinary expertise* → "integrated throughout the technology's life cycle"
FAIR[2] data + automated data threads → heavy use of metadata, daily data refresh for scalability.	6) *Data governance & documentation* → "[data provenance, processing are traceable and verifiable]"

1) RAG: retrieval-augmented generation; https://arxiv.org/pdf/2005.11401
2) FAIR: findable, accessible, interoperable, reusable; https://www.nature.com/articles/sdata201618.pdf

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Case Study #2
Virtual Clone – Automated AI-Enabled Clone Selection

Virtual Clone: performs 10% better than SMEs on a subset of drug modalities.

AI solution characteristics	FDA principles anchored
FAIR[1] data + automated data threads → automated data flows were essential to success… (previous unsuccessful attempts had manual workflow steps).	6) *Data governance & documentation* → "data (…) processing steps, and analytical decisions are documented in a detailed (…) manner"
Multi-modal[2] feature set → images, categorical data, time series, and analytical measurements contribute to prediction accuracy.	7) *Model design & development practices* → "best practices in model and system design and software engineering and leverages data that is fit-for-use"
Rigorous model qualification → governed by two SOPs: 1) AI SOP (based on NIST AI RMF[3]), 2) ML SOP (internal extension of ASME VVUQ 40 standard[4]).	2) *Risk-based approach* / 8) *Risk-based performance assessment* 3) *Adherence to standards* → "AI technologies adhere to relevant (…) technical, scientific (…) standards"

1) FAIR: findable, accessible, interoperable, reusable; https://www.nature.com/articles/sdata201618.pdf
2) https://arxiv.org/pdf/2309.10020
3) https://www.nist.gov/itl/ai-risk-management-framework
4) https://www.asme.org/codes-standards/publications-information/verification-validation-uncertainty

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What We Should Debate Next

A) Determinism is the wrong lens

Manage **variability statistically** (ensembles, repeated runs) and **operationally** (observability, monitoring).

B) Interpretability over explainability

Interpretability (why) is more important than **explainability** (how) → inspect AI's **reasoning traces** and **decision rubrics**.

C) FAIR data is limiting AI value

Trustworthy AI operates on **FAIR data**, which faces significant cultural, infrastructure, and technology challenges.

D) Embrace context engineering

Prompt engineering is obsolete. Effective solutions implement **context engineering** and **systems thinking**.

E) Benchmarks for our industry

Open benchmarks for our **specific domain** are needed → *FrontierScience* for expert scientific reasoning tasks as a source of inspiration.

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Takeaway Messages

AI in CMC is an **engineered system**, not a model

There is "*no silver bullet*", "*no free lunch*", and "the *bitter lesson*" still applies.

Context engineering and **systems thinking** (plus AI **organizational agility**) will distinguish *winners* from *followers*.

1

Trustworthy AI is achievable **now**

Grounding (RAG), "**evals**" (evaluation harnesses), **lifecycle** management, and **change controls** work *today*.

Organizational inertia and **FAIR data** threads are *the limiting step*.

2

Move from pilots to **intelligence at scale**

ROI scales when *strategy*, *data*, *people*, *process*, and *technology* turn **point tools** into durable **integrated solutions**.

3

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