Integrating Digital Data Flow with Generative AI for Enhanced Clinical Trial Automation

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Meet the Speakers

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Title: Product Manager, Life Science Solutions

Organization: Fujitsu Limited

- CDISC Authorized Instructor of XML Technologies since 2015
- Product Manager of Software Products for Life Science Industry, including SDTM Automation and DDF Enablement since 2015

Daisuke Seyama

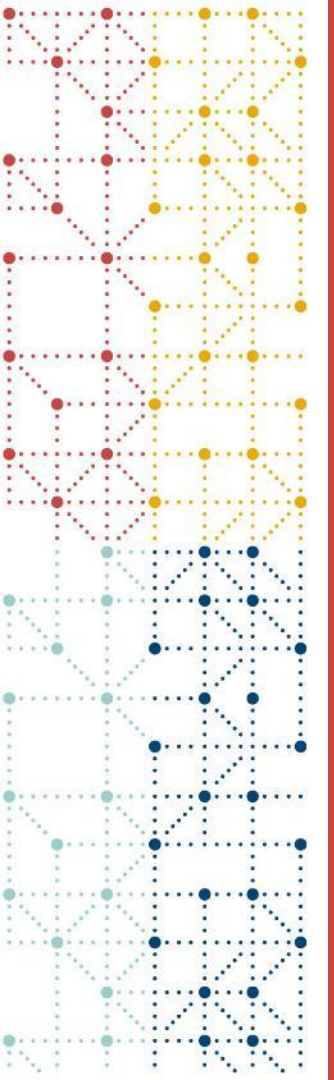
Title: Technology Evangelist, Healthy Living

Organization: Fujitsu Limited

- Specialized in AI Technologies and Cloud Architecture
- Oversees Adoption of Generative AI to DDF Enablement Software since 2023

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of the organization where the author belongs.*



Agenda

1. Benefits and Risks of Generative AI
2. Enabling DDF User Scenarios using SDR and Generative AI

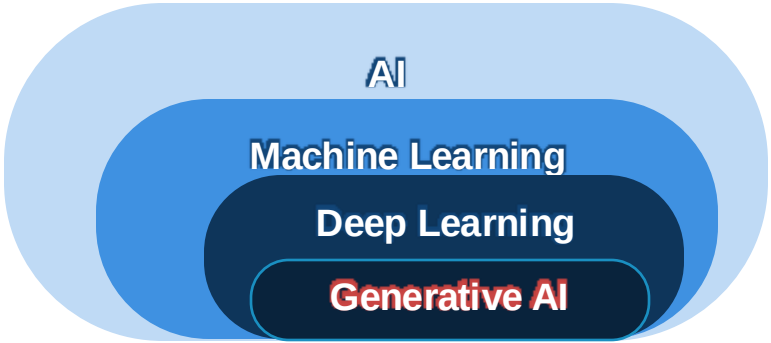
Benefits and Risks of Generative AI

What is Generative AI?

Generative AI is a new AI that can leverage training data to **"generate a variety of new contents"**.

(E.g., Photo created by Stable Diffusion.)

Classification of AI Technologies



"Photo of an Astronaut riding a Horse"
created by Generative AI

Reference: https://en.wikipedia.org/wiki/Stable_Diffusion

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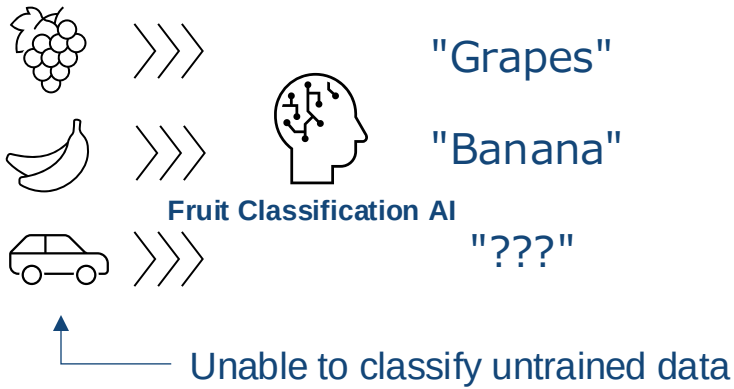
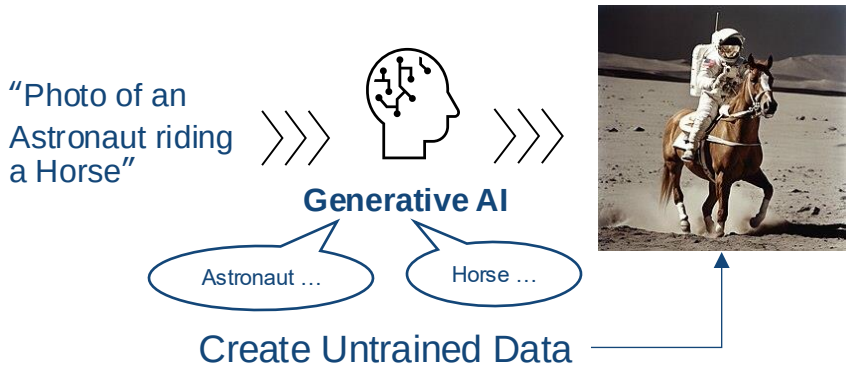
What's different from traditional AI?

- Traditional AI is mostly about classification and prediction within trained patterns or rules.
- Generative AI can create new data based on trained patterns.

Traditional AI



Generative AI



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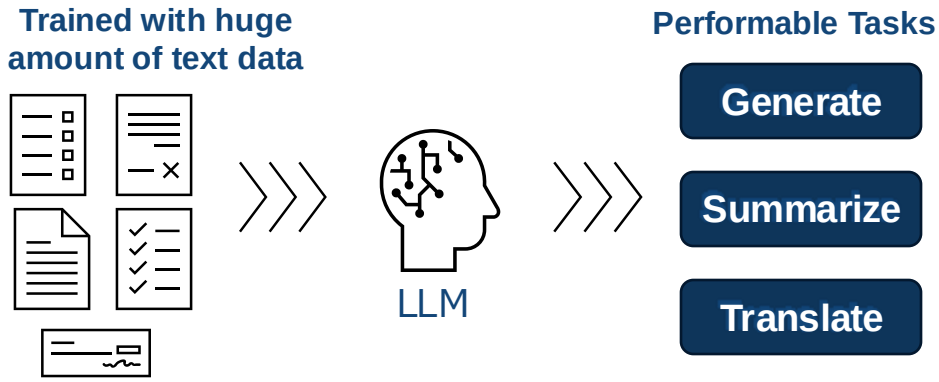
What is LLM?

- Large Language Model (LLM) is a text-generation AI model that has learned huge amounts of text data.
- A single LLM can perform various Natural Language Processing (NLP) tasks, such as summarization or translation.
- You can perform complex tasks such as summarizing long English sentences in Japanese.

* GPT-3 is said to have learned about 4TB of text data.



Summarize Lincoln's Gettysburg Address in Japanese

Four score and seven years ago our fathers brought forth on this continent, a new nation, …

87年前、自由と平等を理念とするアメリカ合衆国が建国された。南北戦争という試練を乗り越え、この国が人民のための政府として永遠に続くことを願う。戦死した兵士たちの犠牲を無駄にせず、自由と平等のために戦い続ける決意を表明する。

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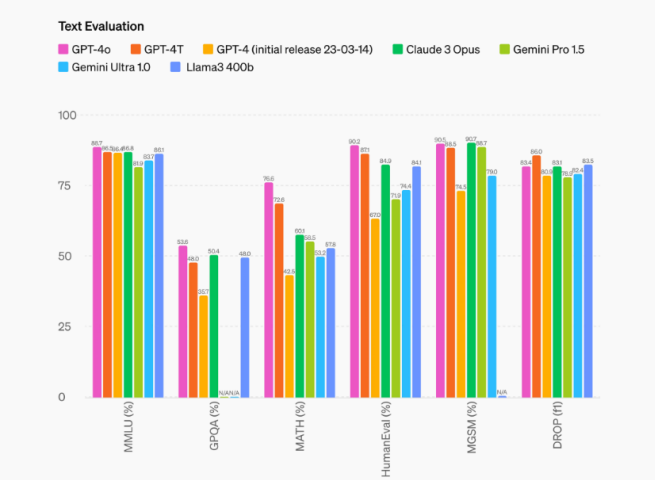
Well-known LLMs

- Since ChatGPT was released in November 2022 with great impact, various LLMs have appeared in the world.
- OpenAI announced GPT-4o, which is announced as outperforming its competitors on various benchmarks.



Reference: Hello GPT-4o | OpenAI

OpenAI

GPT-4o

New flagship model of ChatGPT that supports audio, vision, and text input and responds as quickly as human conversation.

Meta

LLaMA

Open source LLM developed by Meta available for research and customization. Many LLMs based on LLaMA, such as ELYZA of Tokyo University, were born.

Google

Gemini

Previously called Bard, Google's multi-modal generative AI model that supports multiple data types, including text, images, audio, and video.

ANTHROP\C

Claude

LLM developed by American startup Anthropic that scored higher than GPT-4 for some benchmarks.

Fugaku-LLM

LLM developed by various Japanese institutions/companies using Fugaku super-computer that scored highest for Japanese language benchmark.

Performance of LLMs

- Performance of ChatGPT on USMLE (Feb 2023) *1
  - ChatGPT/GPT-3.5 performed at or near the passing threshold for USMLE (United States Medical Licensing Exam) exams without any specialized training or reinforcement.
  - USMLE Program commented on the study that there is "insufficient evidence to support the current claims that AI can pass the USMLE Step exams" because the practice questions used by ChatGPT were not representative of the entire depth and breadth of USMLE exam content. *2
- Performance of Generative Pretrained Transformer on the NMLE in Japan (Jan 2024) *3
  - GPT-4 with optimized prompts achieved a minimum passing scoring rate in the 117th NMLE (National Medical Licensing Exam) in Japan.
  - Certain answers were outdated or critically incorrect in current medical contexts.

References:
*1 PLOS Digital Health: Performance of ChatGPT on USMLE: Potential for AI-assisted medical education using large language models
*2 USMLE Program Discusses ChatGPT
*3 PLOS Digital Health: Performance of Generative Pretrained Transformer on the National Medical Licensing Examination in Japan

Challenges of using LLM

- **"Hallucination"** is a response generated by AI which contains false or misleading information presented as fact.
- Hallucination makes outputs from Generative AI untrustworthy, and thus cannot be ignored to use LLM safely in the real life.

Example 1:

Google announced its new AI bot, Bard, in Feb 2023, but the bot responded with an incorrect answer against a query about the James Webb Space Telescope in their promotion video.

Reference: Google's Bard AI bot mistake wipes $100bn off shares (BBC)

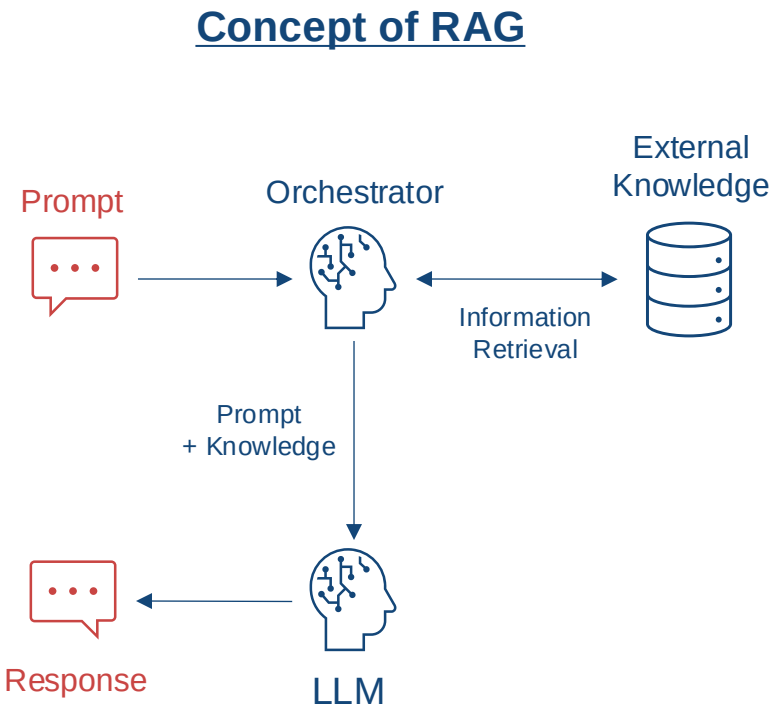
Example 2:

The New York Times wrote in May 2023 that a lawyer used ChatGPT to prepare a court filing and submitted to a federal court, which contained number of court decisions that do not exist.

Reference: Here's What Happens When Your Lawyer Uses ChatGPT (The New York Times)

Techniques to reduce Hallucinations

- A technique called Retrieval Augmented Generation (RAG) adds an information retrieval mechanism to provide LLM with grounding data.
- Based on the RAG concept, such techniques as Adaptive-RAG and HyDE are also emerging.
- Safe use of LLM in the real life requires combining relevant techniques.



Enabling DDF User Scenarios using LLM and Study Definitions Repository

Recap of Digital Data Flow

Values of DDF

- Reduce lag time between protocol approval and study startup
- Reduce cycle time for converting collected data to SDTM
- Reduce manual duplication of effort and increase traceability and re-use

Enabler of DDF

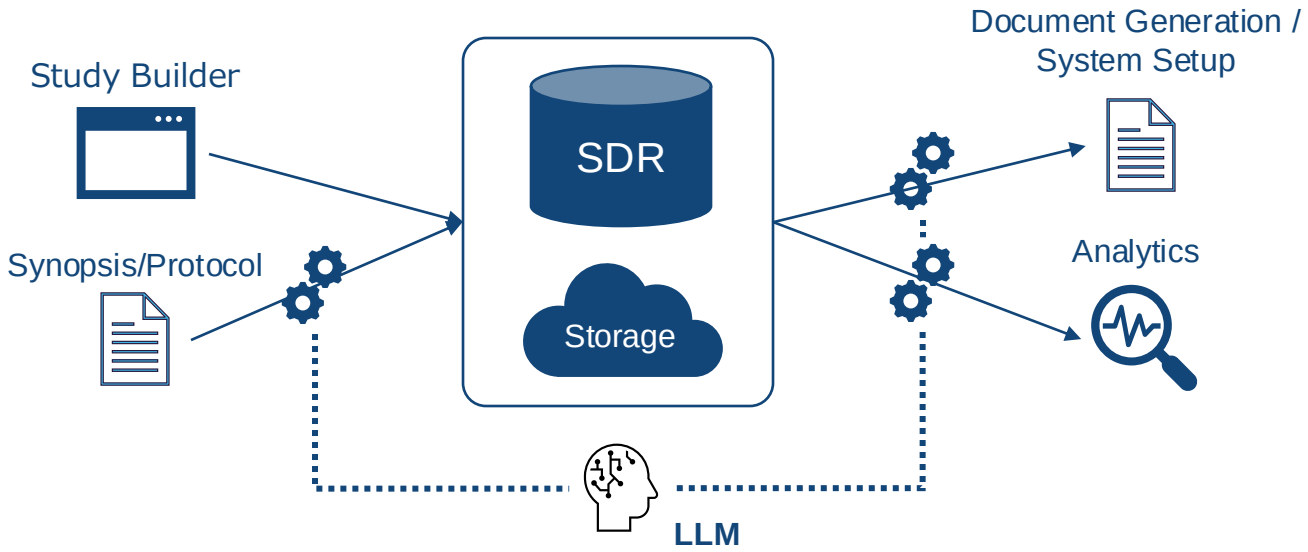
- Clinical Trial Protocol Digitalization

Example User Scenarios

- Reduce efforts and accelerate document authoring by automated generation
- Accelerate study startup and SDTM transformation by automated setup

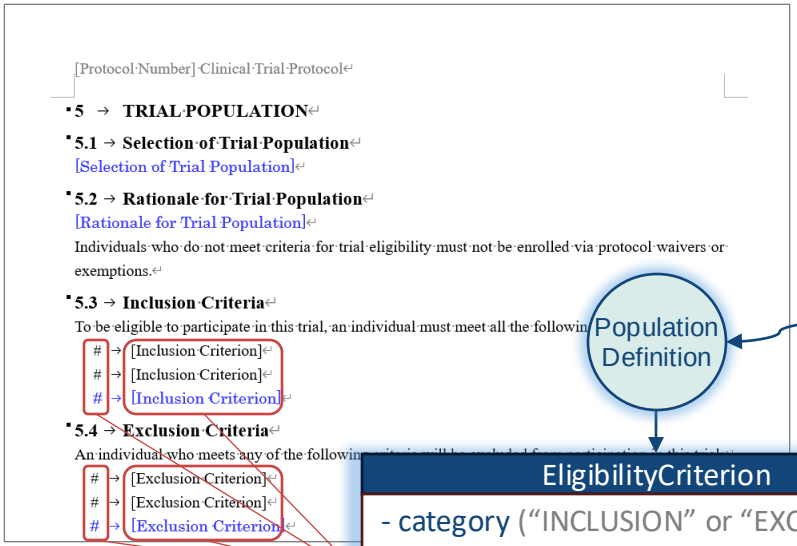
LLM-Powered Digital Data Flow

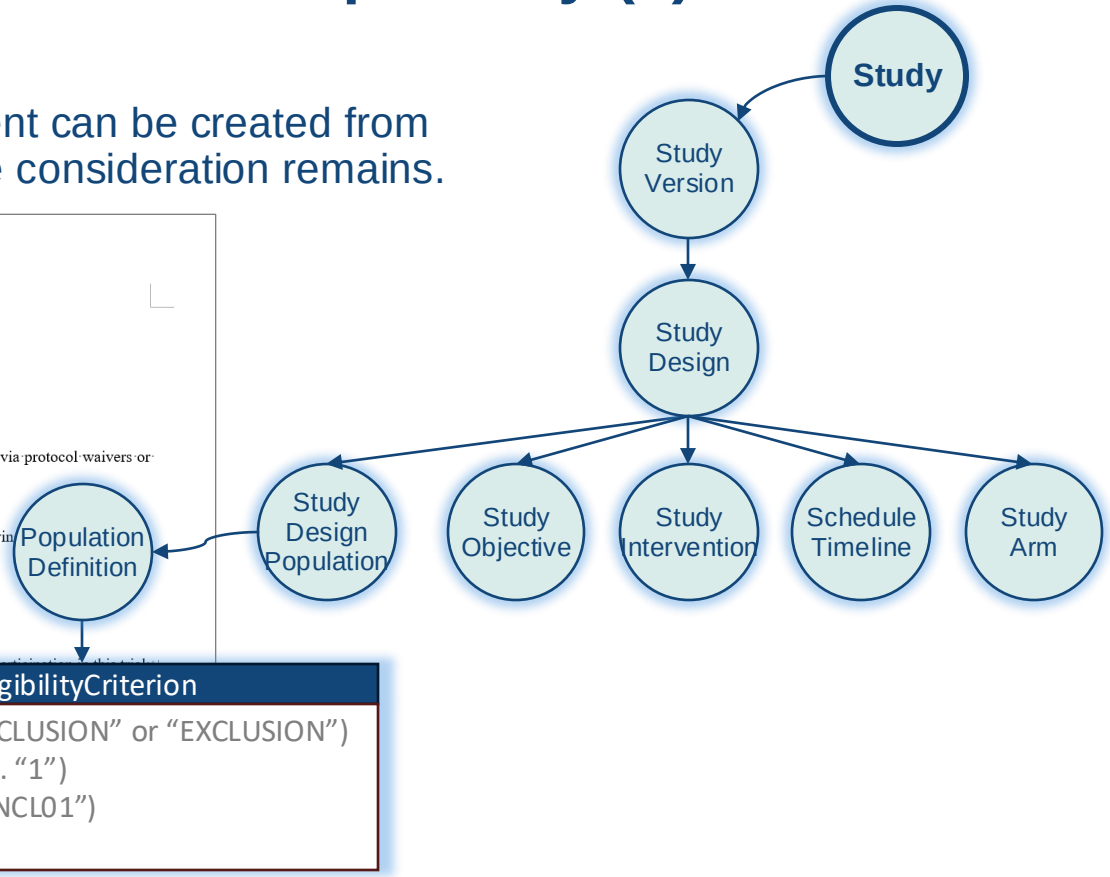
- DDF serves as the orchestrator and the external knowledge source for LLM.



Recap of Study Definitions Repository (1)

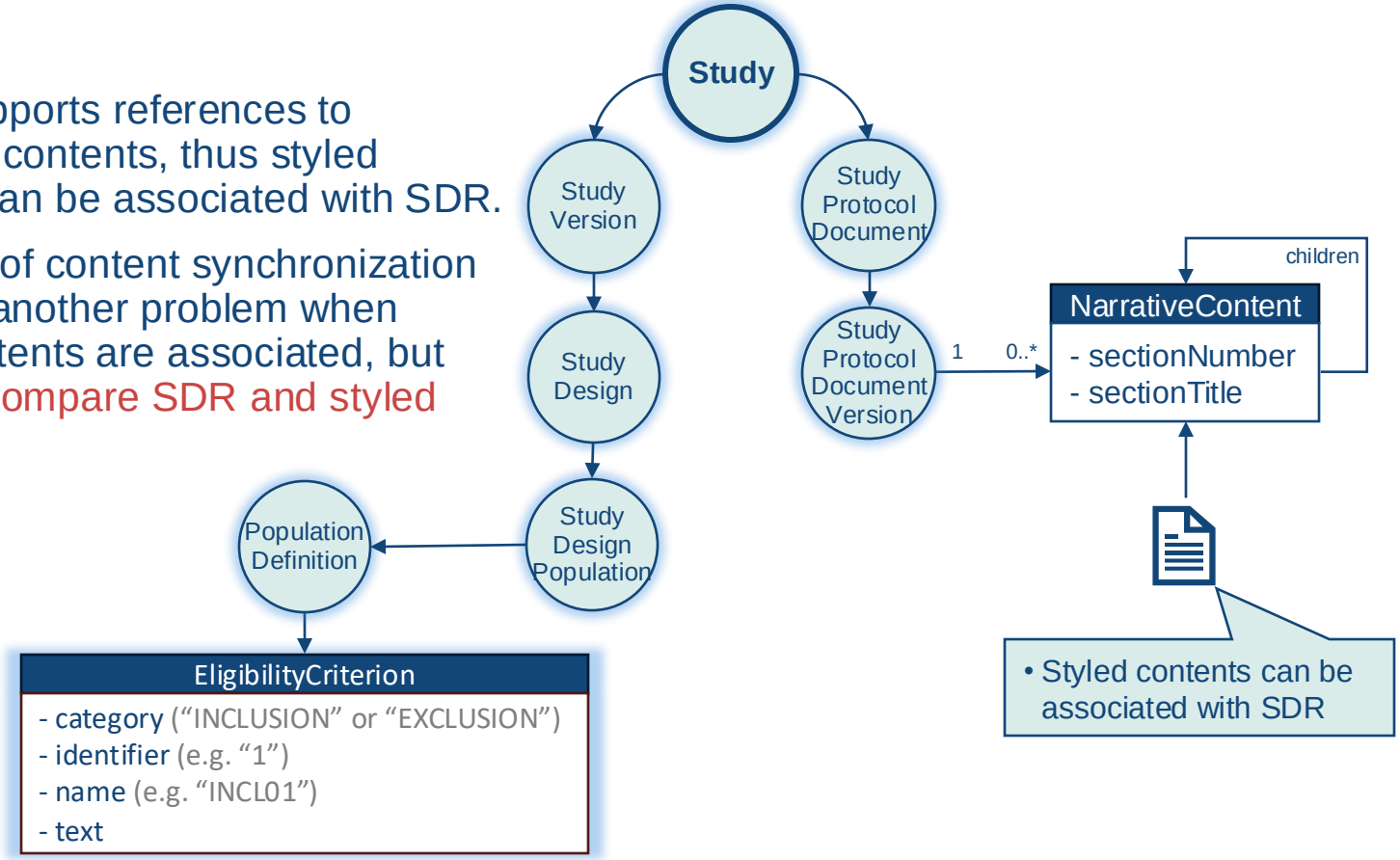
- M11-based protocol document can be created from USDM-based SDR, yet style consideration remains.





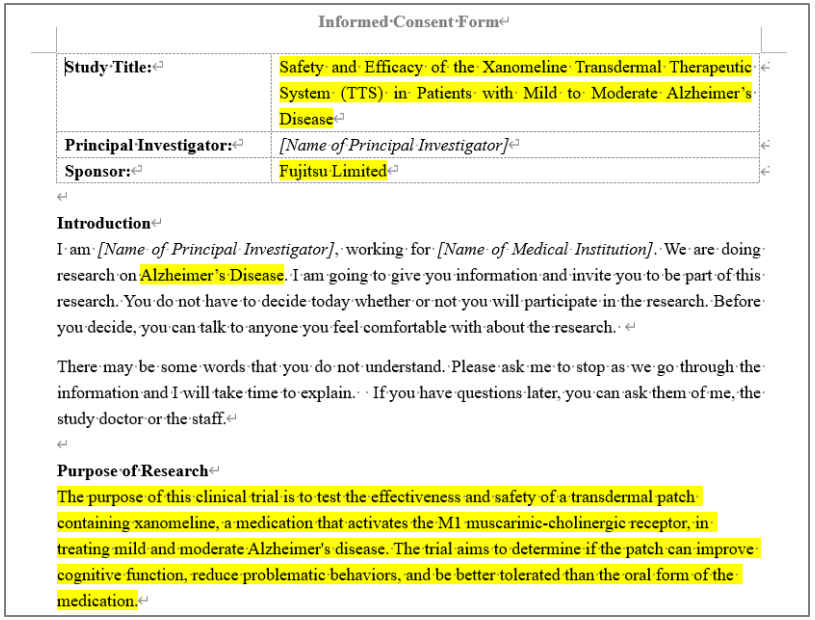
Recap of Study Definitions Repository (2)

- USDM supports references to document contents, thus styled contents can be associated with SDR.
- Validation of content synchronization becomes another problem when styled contents are associated, but LLM can compare SDR and styled contents.



Automated Document Generation

- Document contents may differ in tones and languages from digitized protocol.



Informed Consent Form

Study Title:	Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients with Mild to Moderate Alzheimer's Disease
Principal Investigator:	*[Name of Principal Investigator]*
Sponsor:	Fujitsu Limited

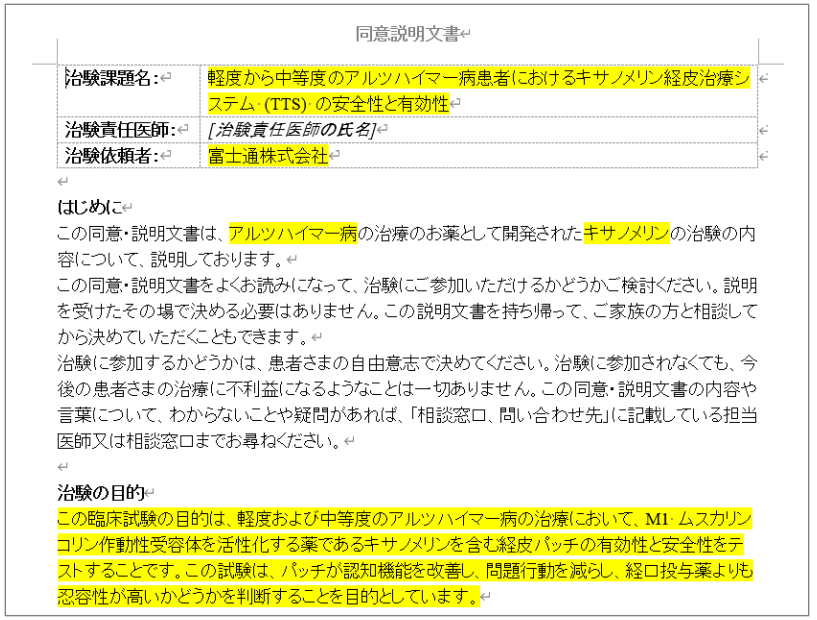
Introduction

I am *[Name of Principal Investigator]*, working for *[Name of Medical Institution]*. We are doing research on Alzheimer's Disease. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.

Purpose of Research

The purpose of this clinical trial is to test the effectiveness and safety of a transdermal patch containing xanomeline, a medication that activates the M1 muscarinic-cholinergic receptor, in treating mild and moderate Alzheimer's disease. The trial aims to determine if the patch can improve cognitive function, reduce problematic behaviors, and be better tolerated than the oral form of the medication.



同意説明文書

治験課題名:	軽度から中等度のアルツハイマー病患者におけるキサノメリン経皮治療システム (TTS) の安全性と有効性
治験責任医師:	*[治験責任医師の氏名]*
治験依頼者:	富士通株式会社

はじめに

この同意・説明文書は、アルツハイマー病の治療のお薬として開発されたキサノメリンの治験の内容について、説明しております。

この同意・説明文書をよくお読みになって、治験にご参加いただけるかどうかご検討ください。説明を受けたその場で決める必要はありません。この説明文書を持ち帰って、ご家族の方と相談してから決めていただくこともできます。

治験に参加するかどうかは、患者さまの自由意志で決めてください。治験に参加されなくても、今後の患者さまの治療に不利益になるようなことは一切ありません。この同意・説明文書の内容や言葉について、わからないことや疑問があれば、「相談窓口、問い合わせ先」に記載している担当医師又は相談窓口までお尋ねください。

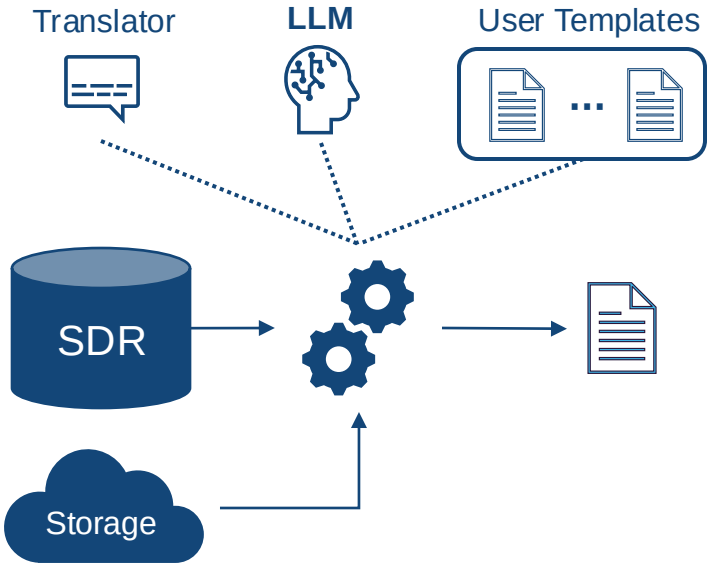
治験の目的

この臨床試験の目的は、軽度および中等度のアルツハイマー病の治療において、M1 ムスカリンコリン作動性受容体を活性化する薬であるキサノメリンを含む経皮パッチの有効性と安全性をテストすることです。この試験は、パッチが認知機能を改善し、問題行動を減らし、経口投与薬よりも忍容性が高いかどうかを判断することを目的としています。

LLM-Powered Automated Document Generation

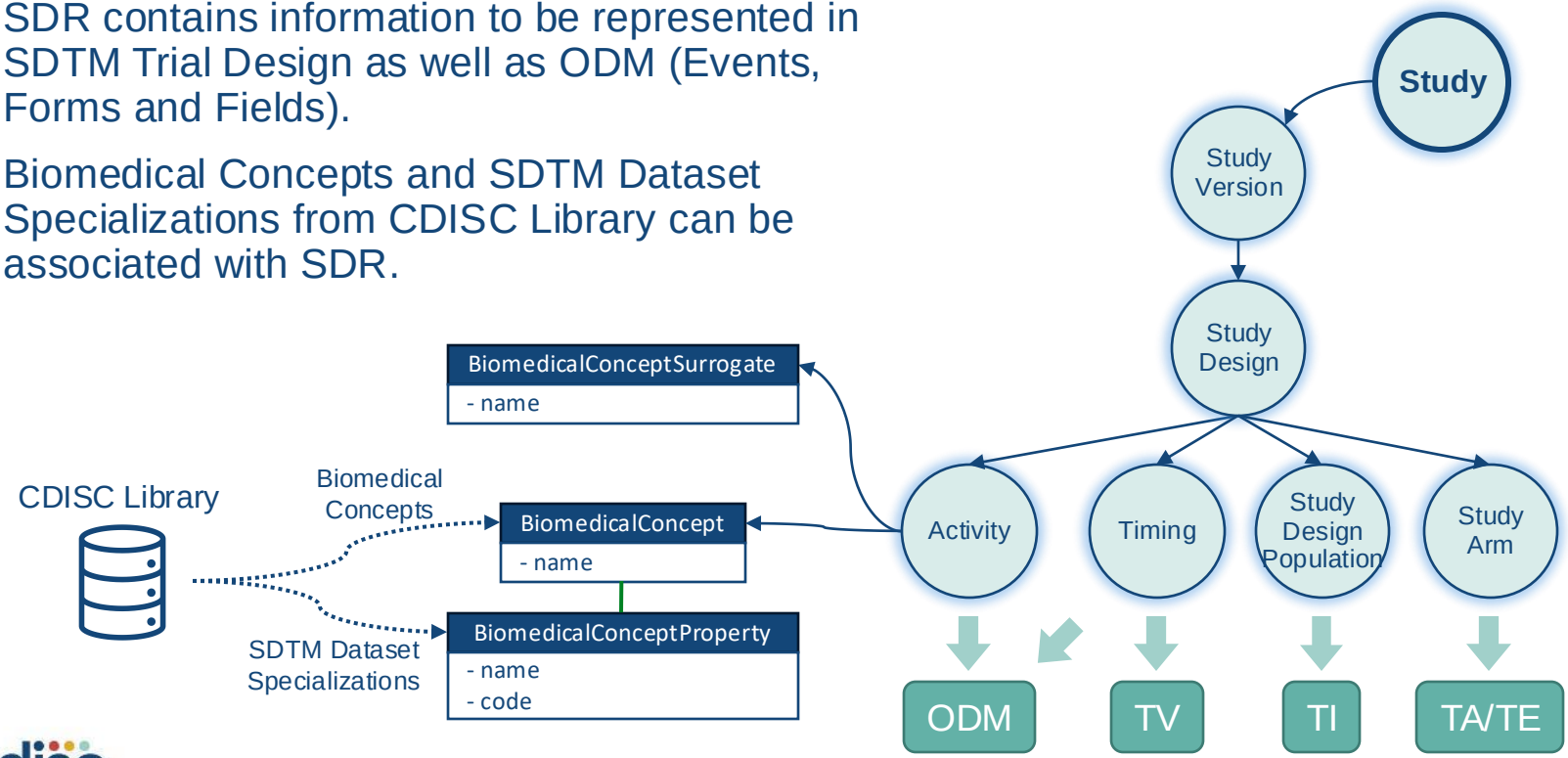
- LLM will enable document generation required in real life with the following functionality.

Functionality	Description
Extract from SDR	Insert properties and styled contents stored in the SDR
Prompt to LLM	Insert response from LLM against user prompt
Language Translation	Insert translated text
Prompt to LLM from External Knowledge	Insert response from LLM against user prompt with external knowledge



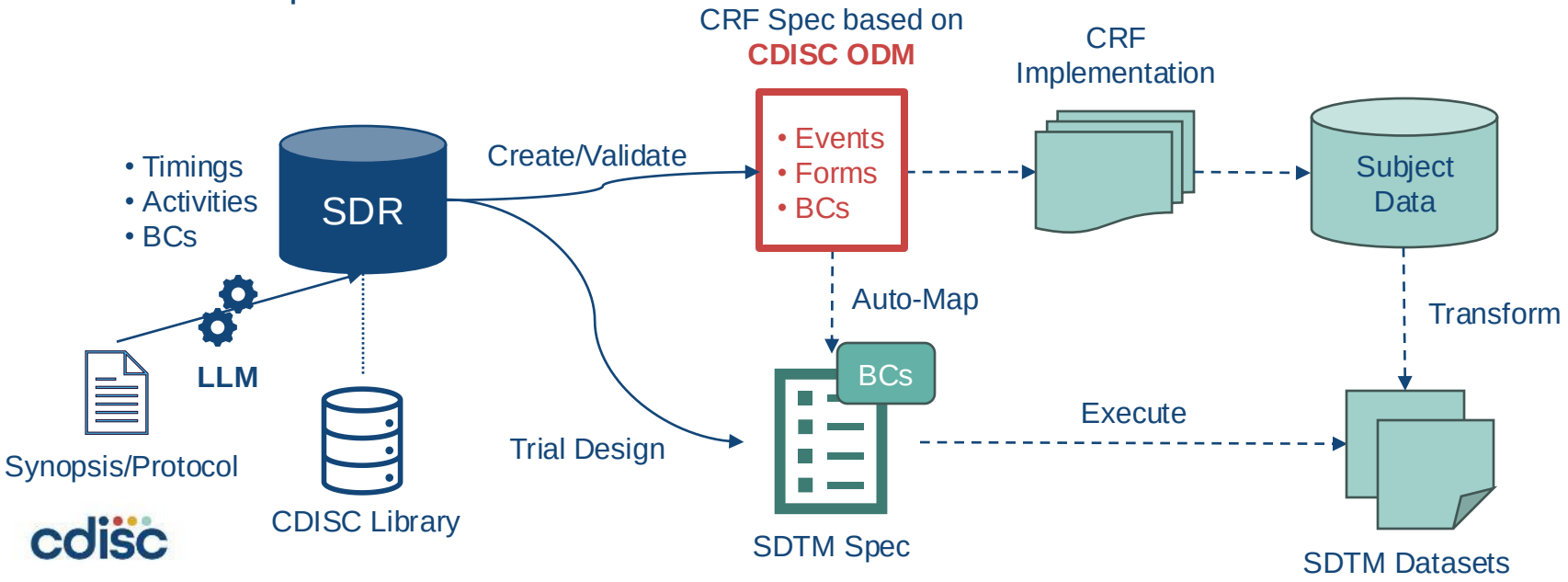
Automated Study Setup and SDTM Transformation (1)

- SDR contains information to be represented in SDTM Trial Design as well as ODM (Events, Forms and Fields).
- Biomedical Concepts and SDTM Dataset Specializations from CDISC Library can be associated with SDR.



Automated Study Setup and SDTM Transformation (2)

- Automated setup of data capturing tools can be achieved by generating ODM-based CRF specification (and then implementation-specific information will be added).
- Automated SDTM transformation can be achieved by synchronizing SDR, CRF spec and SDTM spec.



Summary and Conclusions

- Safe use of LLM in the real life requires use of RAG.
- SDR is an external knowledge for RAG in the case of DDF.
- Real-life automated document generation can be achieved with LLM-powered DDF implementation.
- Regional implementation of ICH M11 will have significant impact to DDF implementation.
- Processes around SDR (when and who will populate SDR contents) will need to be discussed in each organization.

Thank You!

For questions, please contact the speaker at:

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