U.S. FOOD & DRUG ADMINISTRATION

Quality Assessment Modernization: Vision and Future Roadmap

Sau (Larry) Lee, PhD
Deputy Director of Science
Office of Pharmaceutical Quality

Pharmaceutical Quality Symposium:
Quality, Supply Chain & Advanced Manufacturing
October 31, 2023

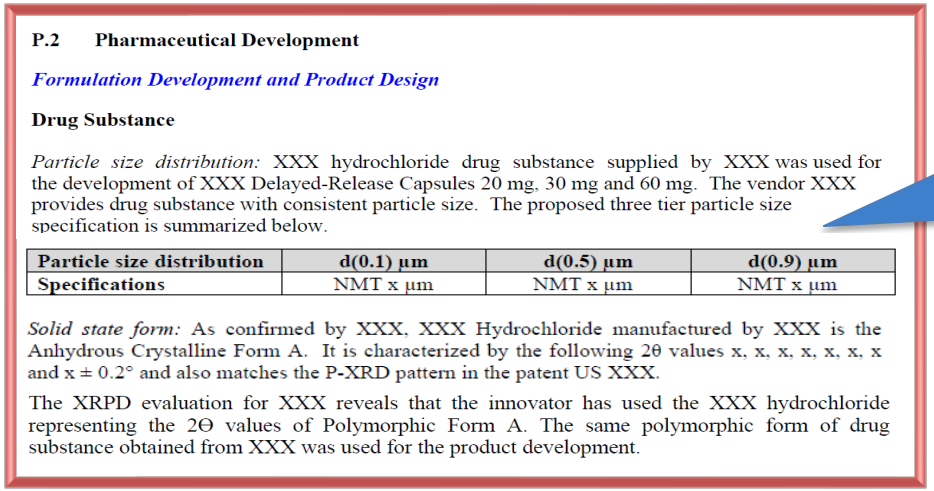

Everyone deserves
confidence in their *next* dose
of medicine.
Pharmaceutical quality
assures the
availability,
safety,
and efficacy
of *every* dose.

Quality Assessment in Office of Pharmaceutical Quality

- Office of Pharmaceutical Quality (OPQ) evaluates how a drug is formulated, how it is manufactured, and the facilities used in the manufacturing process to ensure a safe and effective medication is being delivered to the intended population.
- OPQ also looks at formulation and manufacturing changes made after a drug is approved to ensure quality is maintained throughout the product's lifecycle.

Challenges to Assessing Quality

- There has been an increase in submission number and complexity with accelerated timelines.
- Annually, OPQ reviews ~ 3,000 INDs, ~240 NDAs/BLAs, ~900 ANDAs, ~10,000 supplements, submitted in **unstructured** PDF format.



P.2 Pharmaceutical Development

Formulation Development and Product Design

Drug Substance

Particle size distribution: XXX hydrochloride drug substance supplied by XXX was used for the development of XXX Delayed-Release Capsules 20 mg, 30 mg and 60 mg. The vendor XXX provides drug substance with consistent particle size. The proposed three tier particle size specification is summarized below.

Particle size distribution	d(0.1) µm	d(0.5) µm	d(0.9) µm
Specifications	NMT x µm	NMT x µm	NMT x µm

Solid state form: As confirmed by XXX, XXX Hydrochloride manufactured by XXX is the Anhydrous Crystalline Form A. It is characterized by the following 2θ values x, x, x, x, x, x, x and x ± 0.2° and also matches the P-XRD pattern in the patent US XXX.

The XRPD evaluation for XXX reveals that the innovator has used the XXX hydrochloride representing the 2Θ values of Polymorphic Form A. The same polymorphic form of drug substance obtained from XXX was used for the product development.

Section P.2 in this actual example contains 9 pages of freestyle narrative in unstructured text

Challenges to Assessing Quality

A freestyle narrative-based quality assessment means:

- unstructured information;
- a summarization of application information; and
- "copy & paste" data

Such system can result in:

- Risk assessment and evaluation of the applicant's mitigation approaches dispersed in lengthy text;
- Inconsistency and ineffectiveness, and encumbered ability to share knowledge and efficiently manage FDA's repertoire of approved drug products and facilities;
- Hindered decision-making capabilities because assessors evaluate each application in relative isolation without fully assessing the wealth of information at FDA's disposal.

Advancing Forward

- For a regulatory assessment focused on quality (Chemistry, Manufacturing, and Controls), a lifecycle approach that underscores good knowledge management is essential.
- To be most efficient, OPQ needs to take advantage of modern IT tools and platforms that:
  - Emphasize structured data* and the ability to capture critical information;
  - Enable a systematic approach to risk assessment, resulting in a more consistent high-quality evaluation and decision making.

* **Structured data** is highly specific and is stored in a predefined format, where **unstructured data** is a conglomeration of many varied types of data that are stored in their native formats.

Advancing Forward

We recognize the need to modernize

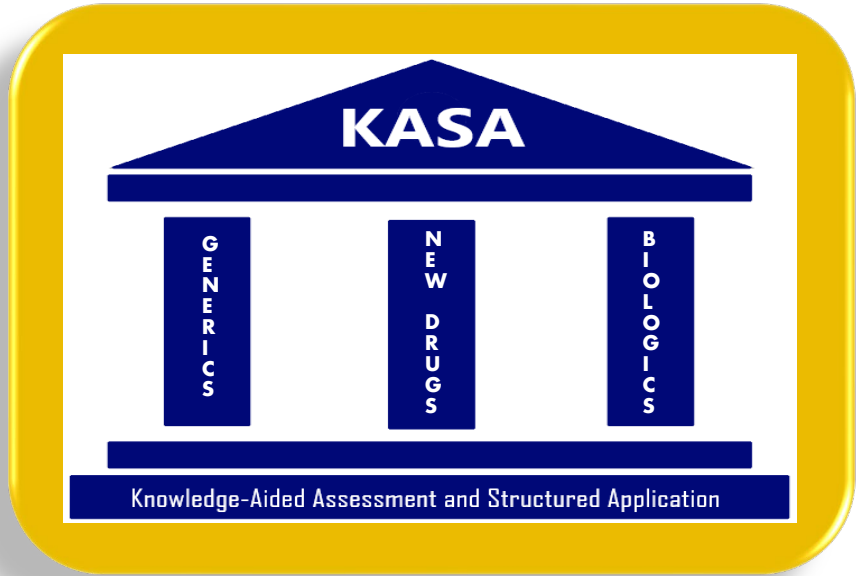
(20th → 21st century technology)

Quality Assessment

moves from narrative information to **structured data and systematic approach for risk assessment powered by IT tools** to best capture/manage knowledge

This concept was envisioned in 2016 and discussed at the Pharmaceutical Science and Clinical Pharmacology Advisory Committee meeting on September 20, 2018, as KASA.

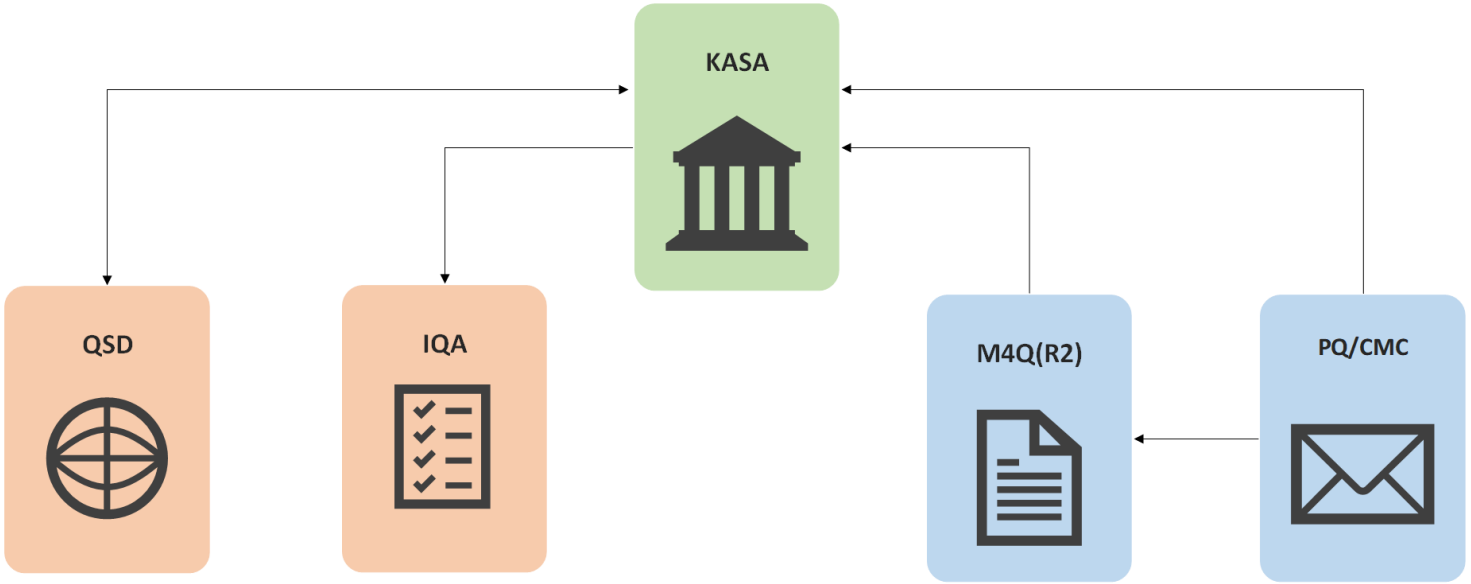
Quality Assessment Transformation: KASA



A data-based platform for structured quality assessments and applications that supports knowledge management

KASA = **K**nowledge-aided **A**ssessment and **S**tructured **A**pplication

How does KASA Connect to other Relevant OPQ Initiatives/Programs?



What is KASA?

Knowledge-Aided Assessment and Structured Application

- Captures and manages knowledge during lifecycle
- Establishes rules and algorithms for risk assessment, control and communication for product, manufacturing, and facilities
- Performs computer-aided analyses
- Provides framework for a structured quality assessment

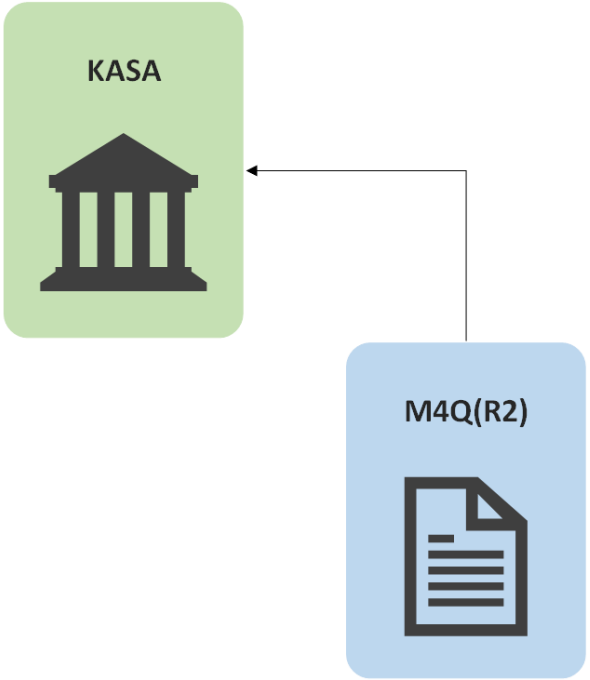
KASA Overview

What is ICH M4Q(R2)?

The Common Technical Document – Quality

- Modernize and optimize the Common Technical Document (CTD) Quality section in Modules 2 and 3
- Incorporate ideas presented in International Council for Harmonisation (ICH) Q8-14 and promoting emerging concepts
- Address regional diversity in requirements
- Organize the information in a structured format to promote knowledge management

KASA Connection to M4Q

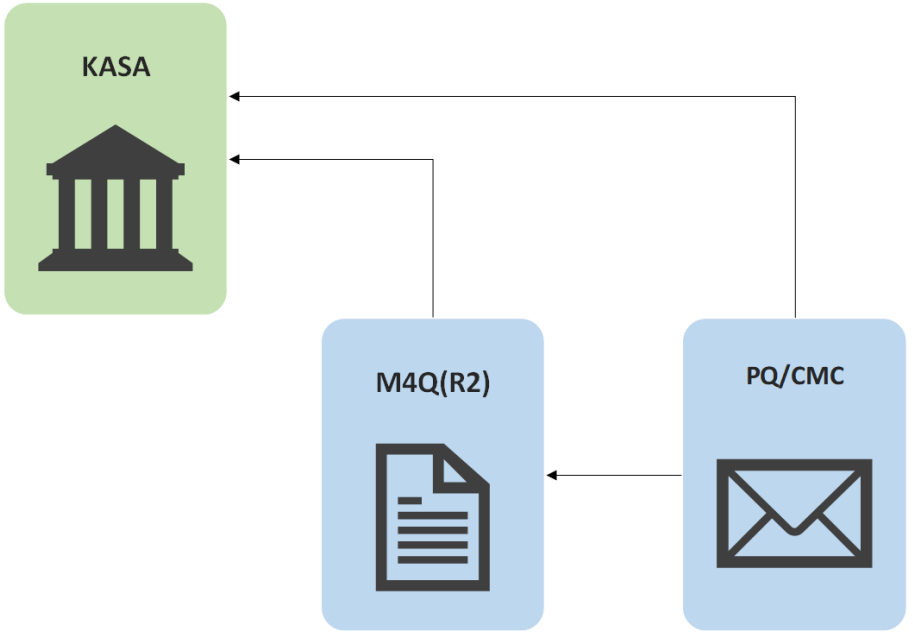


What is PQ/CMC?

Pharmaceutical Quality/Chemistry Manufacturing and Controls

- Establish electronic standards for submitting PQ/CMC data
- Develop structured data standards for PQ/CMC
- Implement a data exchange standard for submitting PQ/CMC data

KASA Connection to PQ/CMC

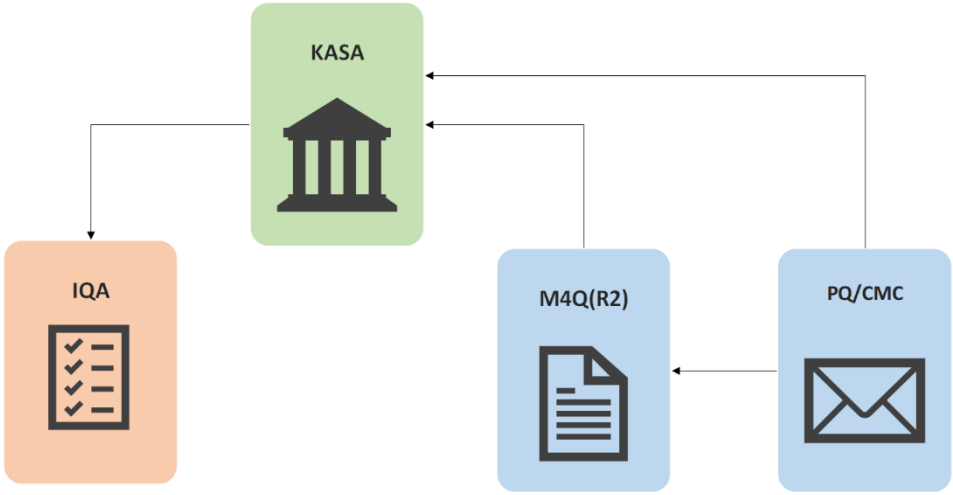


What is IQA?

Integrated Quality Assessment

- Ensure effective and efficient assessment of drug applications by multi-disciplinary teams
- Define business process and operational workload distribution
- Delineate roles and responsibilities
- Establish internal milestones/timelines to meet user fee commitments

KASA Connection to IQA

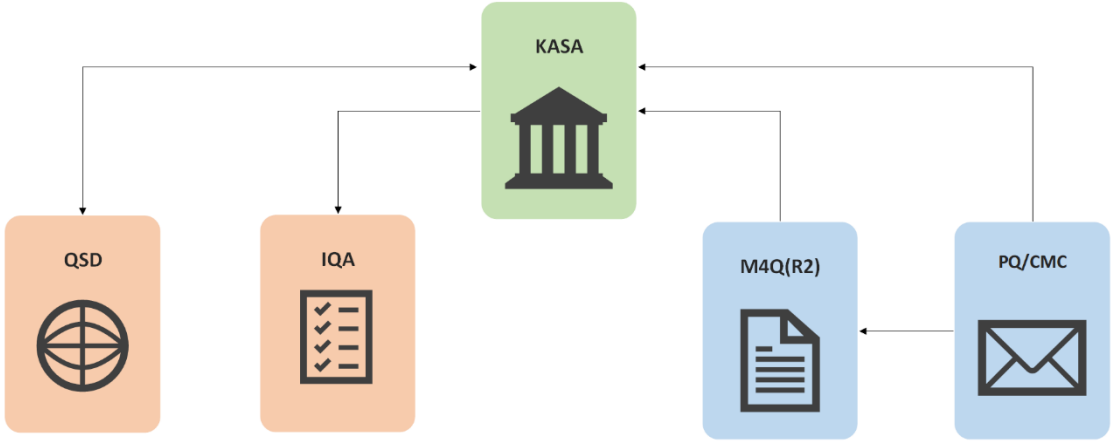


What is QSD?

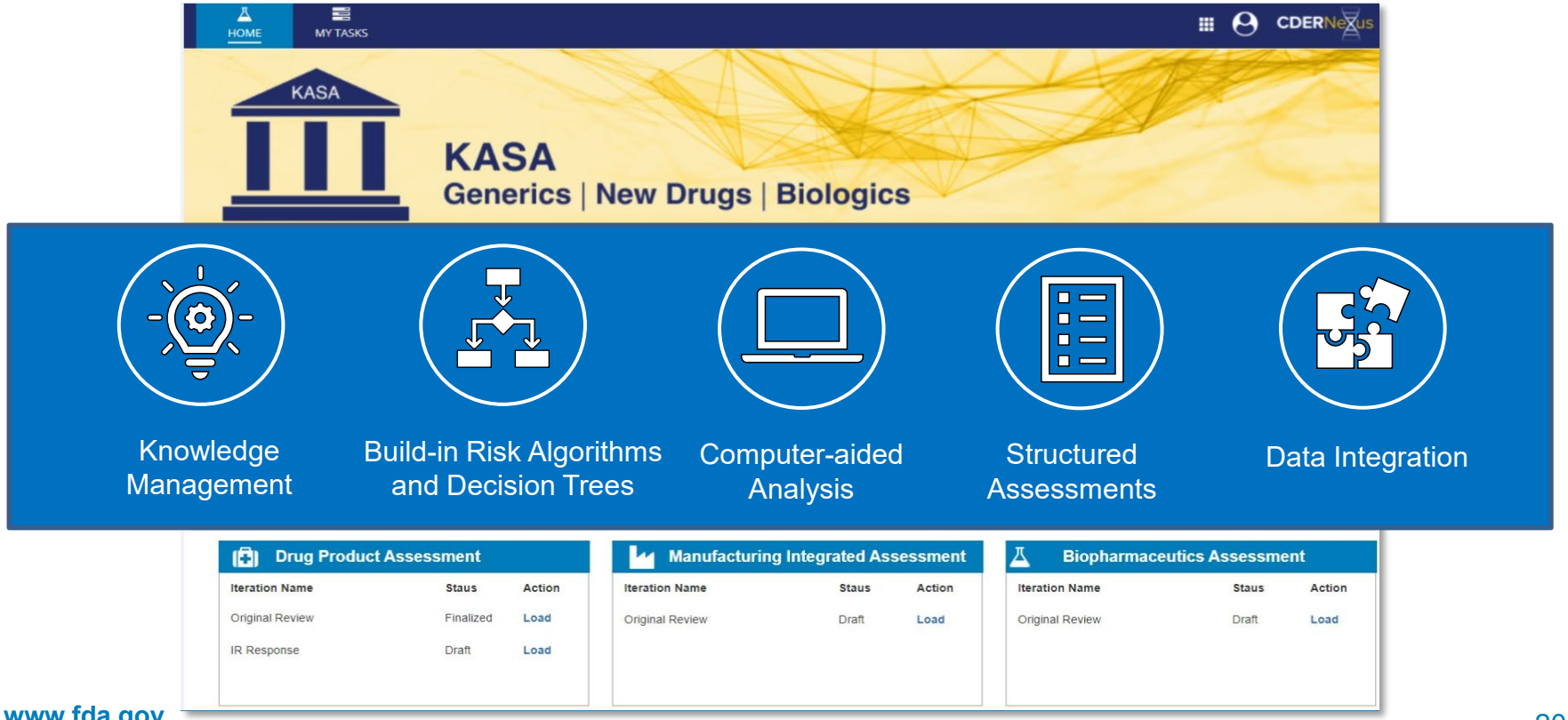
Quality Surveillance Dashboard

- Provide framework for consistent evaluation of facilities and potential quality signals within a product's lifecycle
- Incorporate interactive visualizations that enable users to discover and share insights regarding facilities, manufacturing capabilities, and product quality issues
- Utilize predictive analytics and natural language processing to enable efficient and risk-based assessments
- Integrate and govern facility and postmarket product quality data from across multiple systems

KASA Connection to QSD



KASA for generic solid oral dosage forms is live as of Feb 2021



Plans for KASA's Future

OPQ is focused on continuing KASA's development (creation, testing, refinement) and expanding it to include:

- Drug Substances (for new and generic drugs)
- Liquid-based dosage forms for generics
- INDs
- NDAs
- BLAs
- Post-Approval Supplements (ANDAs, NDAs, BLAs)

Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting on Nov 2-3, 2022

The committee voted unanimously in support of expanding KASA from generic drugs to new drugs and biologics.

Conclusion

- The KASA system enables the use of 21st century technology and is driving innovation for FDA.
- KASA has been successful thanks to the efforts of countless OPQ employees, OBI staff, and contractors, plus the steady support of CDER leadership.

Thank You

U.S. FOOD & DRUG ADMINISTRATION

Effective leadership Collaborative relationships

Encourage innovation **Risk-based approaches**

One Quality Voice

Patients first Team-based processes

Developing and utilizing staff expertise

Scientifically-sound quality standards