Co-Processed APIs

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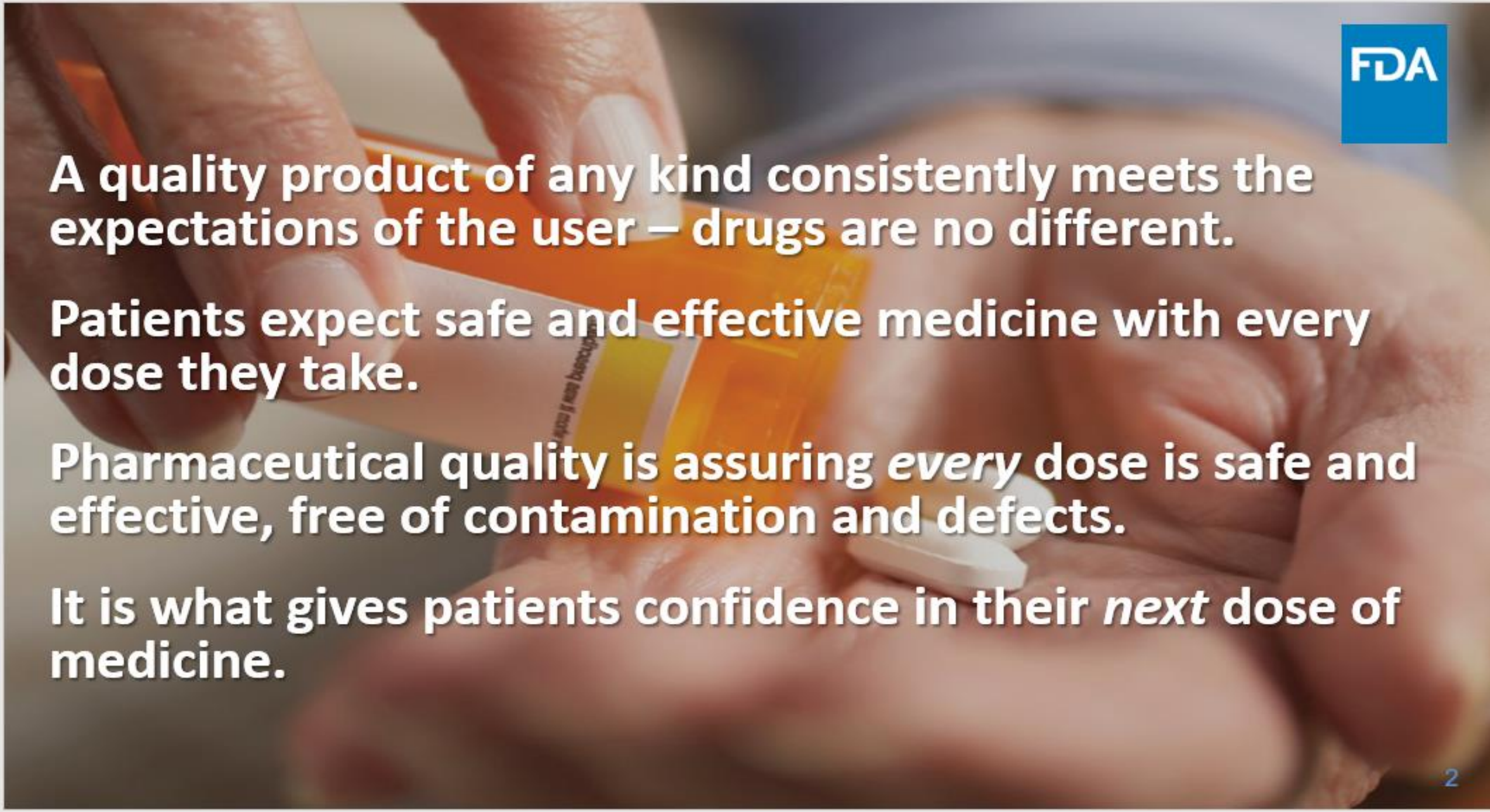

FDA
A quality product of any kind consistently meets the expectations of the user – drugs are no different.
Patients expect safe and effective medicine with every dose they take.
Pharmaceutical quality is assuring *every* dose is safe and effective, free of contamination and defects.
It is what gives patients confidence in their *next* dose of medicine.
2

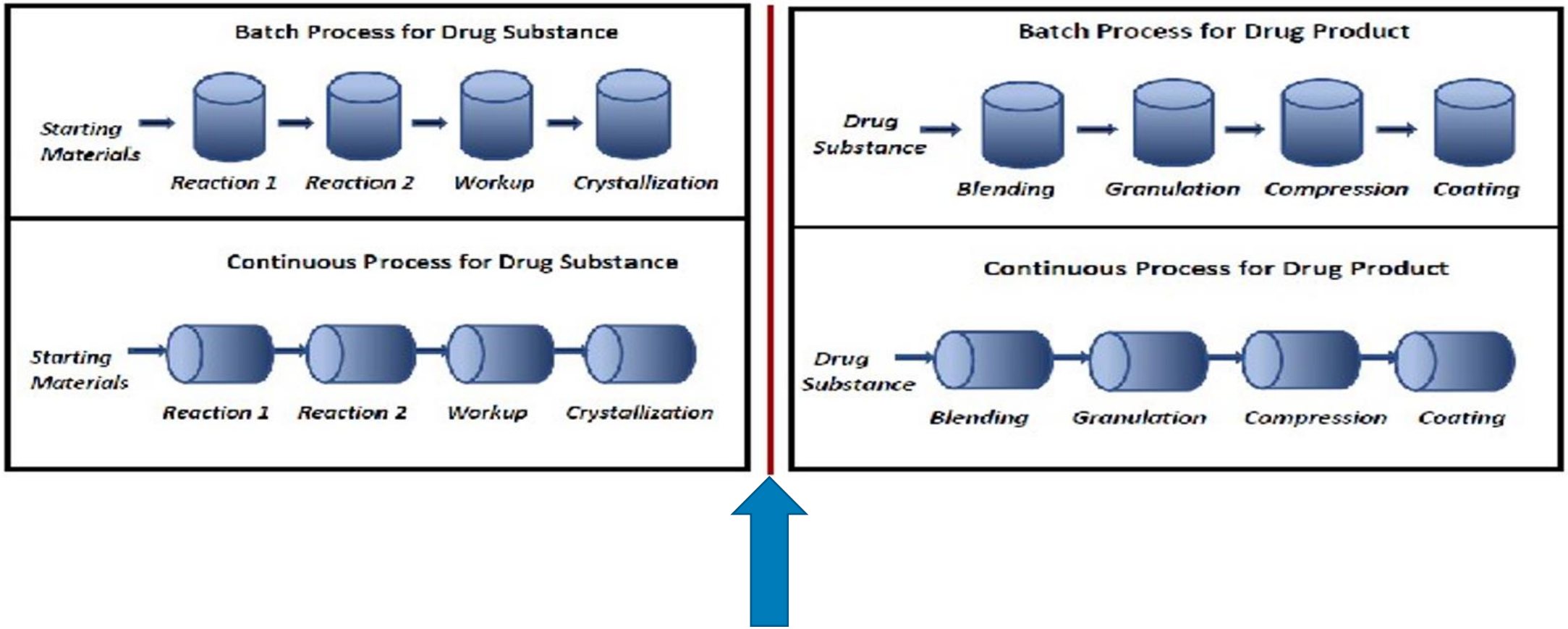
Conference Goal and Format

- Goal:
  - To have discussion around the scientific and regulatory opportunities and challenges that use of co-processed APIs present with the ultimate goal of ensuring that quality medicines are available to American public.
- Format:
  - Podium presentations
    - Opportunities and challenges
    - Case studies about available technologies
  - Breakout sessions for discussions
    - Summary from breakout session
  - Plan to publish the workshop proceedings in J. Pharm. Sci.

Program Highlights

- Main session themes
  - Why does the development pipeline need technology options
  - Technical considerations for designation of co-processed API as drug substance or drug product intermediate
  - Regulatory and scientific considerations for designation of co-processed APIs as drug substance or drug product intermediates
  - How might we advance global harmonization

Small Molecule Manufacturing Process



Co-processed API

Definitions

- Drug Substance (21CFR 314.3):
  - Drug substance is an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body but does not include intermediates used in the synthesis of such ingredient
- Information needed (314.5(d)(1)(i)
  - A full description of the drug substance including its physical and chemical characteristics and stability; the name and address of its manufacturer; the method of synthesis (or isolation) and purification of the drug substance; the process controls used during manufacture and packaging; and the specifications necessary to ensure the identity, strength, quality, and purity of the drug substance and the bioavailability of the drug products made from the substance, including, for example, tests, analytical procedures, and acceptance criteria relating to stability, sterility, particle size, and crystalline form.

Definitions (contd.)

- Drug Product (21CFR 314.3):
  - is a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.
- Information needed (314.5(d)(1)(ii)
  - A list of all components used in the manufacture of the drug product (regardless of whether they appear in the drug product) and a statement of the composition of the drug product; the specifications for each component; the name and address of each manufacturer of the drug product; a description of the manufacturing and packaging procedures and in-process controls for the drug product; the specifications necessary to ensure the identity, strength, quality, purity, potency, and bioavailability of the drug product, including, for example, tests, analytical procedures, and acceptance criteria relating to sterility, dissolution rate, container closure systems; and stability data with proposed expiration dating.----

Definitions (contd.)

- Re-test period(ICH Q1A (R2)):
  - The period of time during which the drug substance is expected to remain within its specification and, therefore, can be used in the manufacture of a given drug product, provided that the drug substance has been stored under the defined conditions. After this period, a batch of drug substance destined for use in the manufacture of a drug product should be re-tested for compliance with the specification and then used immediately. A batch of drug substance can be re-tested multiple times and a different portion of the batch used after each re-test, as long as it continues to comply with the specification. For most biotechnological/biological substances known to be labile, it is more appropriate to establish a shelf life than a re-test period. The same may be true for certain antibiotics.

Definitions (contd.)

- 21 CFR 211.111: (Production time limits)
- When appropriate, time limits for the completion of each phase of production shall be established to assure the quality of the drug product. Deviation from established time limits may be acceptable if such deviation does not compromise the quality of the drug product. Such deviation shall be justified and documented.
  - Typically, specific use time limit is assigned to in-process materials during drug product manufacturing. This is done based on the risk-based evaluation of material's critical quality attributes that can impact the quality of the final drug product, stability of the in-process material and available supporting data.
  - In-process materials used within the established time
- Shelf-life (expiration dating period)(ICH Q1A (R2))
  - The time period during which a drug product is expected to remain within the approved shelf-life specification, provided that it is stored under the conditions defined on the container label

Planning Committee

- **Llorente Bonaga:** Merck & Co. Inc., Regulatory CMC
- **Peter Capella:** Director, FDA, CDER/OPQ/OLDP/Division of Immediate and Modified Release Drug Products II
- **Olivier Dirat:** Pfizer R&D UK Ltd, Advisory Office in Reg CMC
- **Deniz Erdemir:** Bristol Myers Squibb, Material Engineering and Engineering (Drub Product Development)
- **Steven Ferguson:** UCD, Lead for Manufacturing Team for SSPC
- **Stephen W. Hoag:** University of Maryland, Prof. School of Pharmacy, Pharmaceutical Sciences
- **Ephrem Hunde:** FDA, Office of Pharmaceutical Manufacturing Assessment
- **Deborah Johnson:** Branch Chief, FDA/CDER/OPQ/ONDP/Division of Lifecycle API
- **Billie Kline:** Vertex, Engineering and Materials Science (Drug Substance Process and Crystallization)
- **Ivan Marziano:** Pfizer R&D UK Ltd, Crystallization Technology
- **Jeremy Merritt:** Lilly, Particle Design Lab, IQ Co-Processed API WG co-lead
- **Sharon Page:** Pfizer R&D UK Ltd, GCMC
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- **Yihan Wang:** University of Maryland, School of Pharmacy
- **Haitao Zhang:** Sunovion, Associate Research Fellow, Chemical Process R&D