Office of Pharmaceutical Quality: Policy Update

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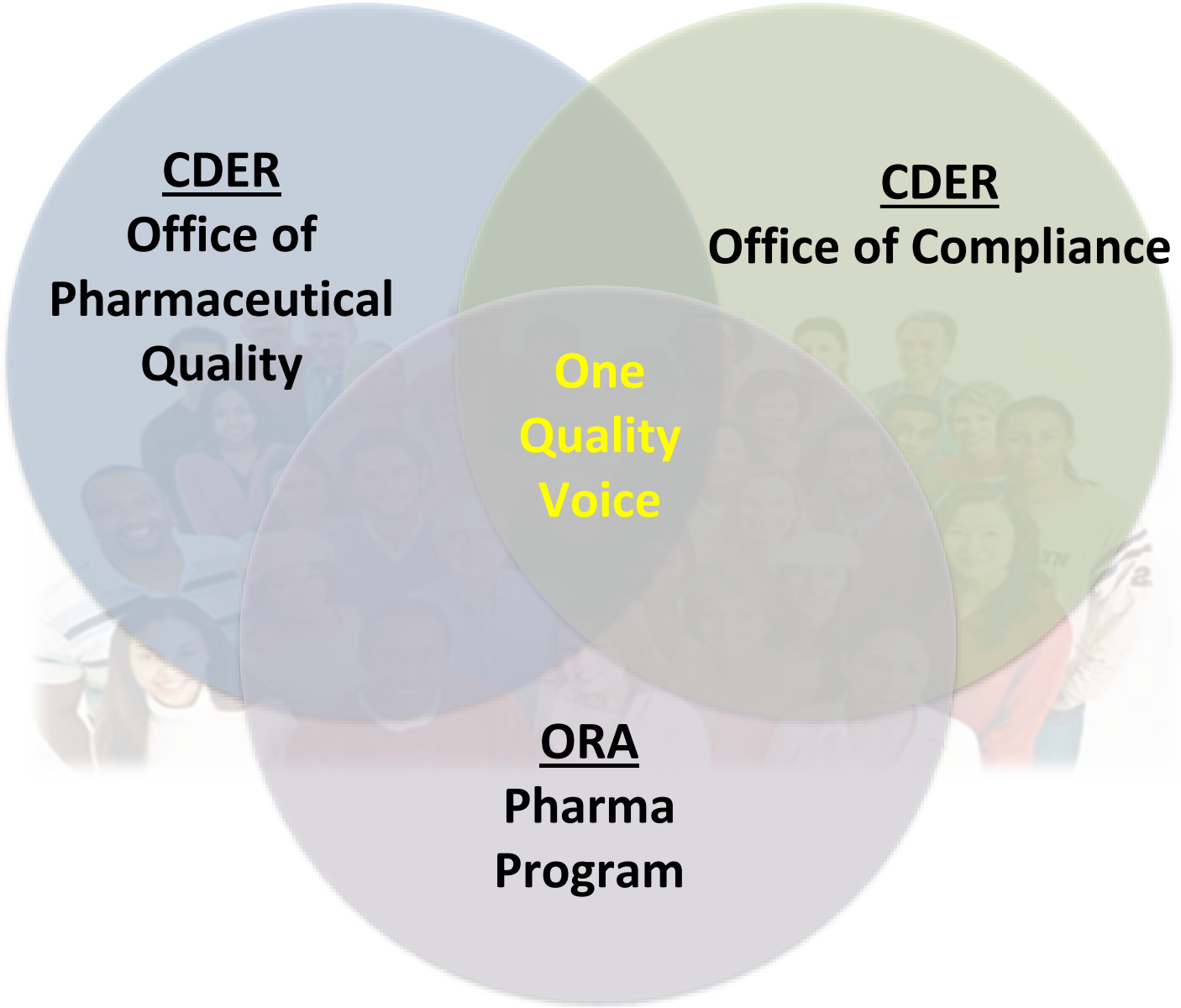
OPQ/CDER/FDA

Generic Drug Forum
April 11, 2018

Outline

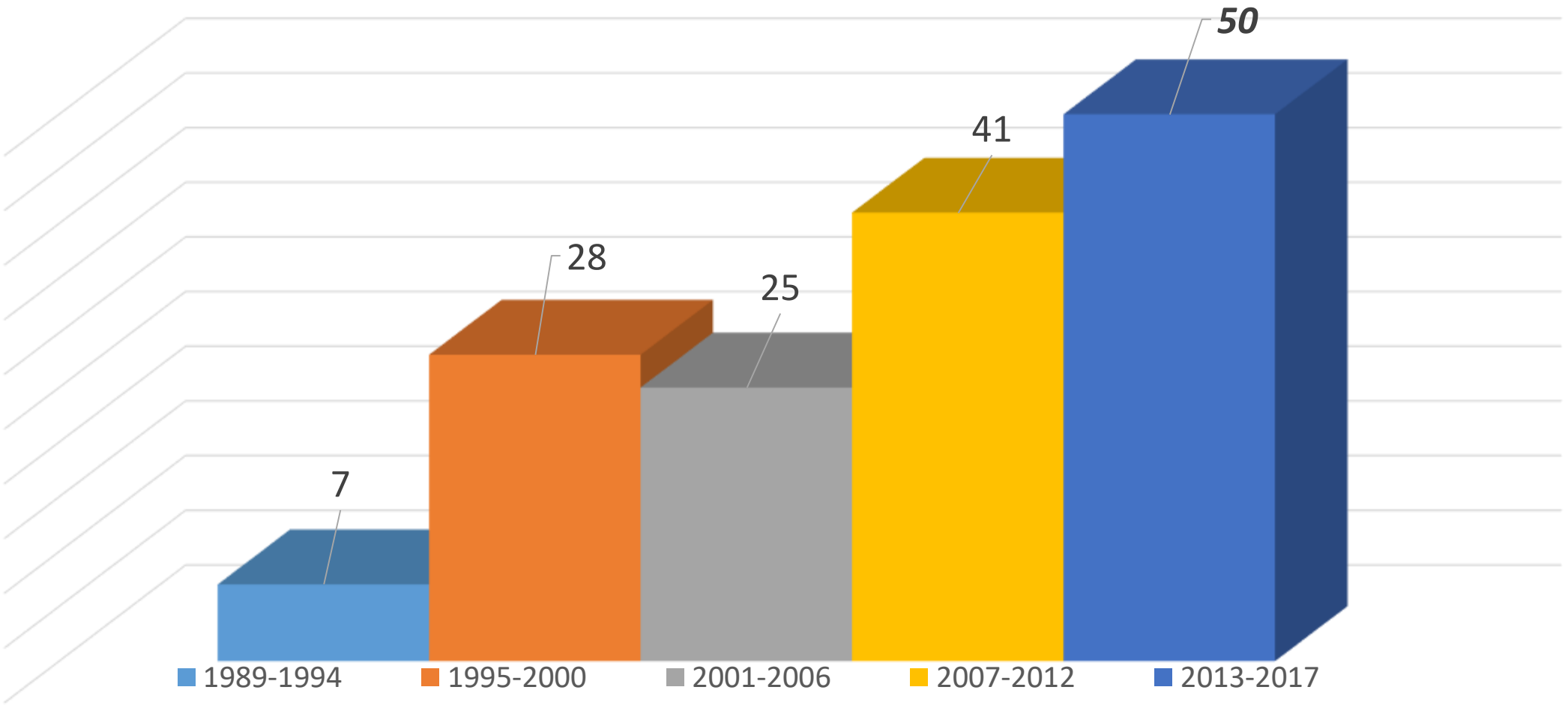
- Quality Policies
  - Recent accomplishments
  - On-going work and priorities
- Strengthen Partnerships and Engage Stakeholders
  - International and Standard-Development Organizations
  - Partnerships with other National Regulatory Agencies

One Quality Voice



Quality Policies: Collaborate and Communicate

Final *Quality-Related* Guidance Since 1989



Quality Policy Activities in 2017

- Published **7 MAPPs (Manual of Policies & Procedures)**
- Responded to **220 external inquiries**
- Responded to **527 Controlled Correspondence**
- Published **10 guidance documents (final and draft)**
  - ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications
  - Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization (Final)
  - CMC Post-approval Manufacturing Changes for Specified Biological Products To Be Documented in Annual Reports
  - Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products
  - Child-Resistant Packaging Statements in Drug Product Labeling
  - Current Good Manufacturing Practice for Medical Gases
  - Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles
  - Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System
  - Drug Products, Including Biological Products, that Contain Nanomaterials
  - Gluten in Drug Products and Associated Labeling Recommendations

Quality Policy Activities in 2017 (cont.)

FOOD AND DRUG ADMINISTRATION

COMPLIANCE PROGRAM | PROGRAM | 7356.002

CHAPTER 56: DRUG QUALITY ASSURANCE

SUBJECT: DRUG MANUFACTURING INSPECTIONS	IMPLEMENTATION DATE
Revision Note: Program revised to add potential OAI reporting responsibilities and to align with the CDER and ORA agreement, Concept of Operations for Facility Evaluation and Inspection.	10/31/2017
	COMPLETION DATE 10/31/2020

DATA REPORTING

PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
All Human Drugs	**Domestic/Foreign surveillance inspections covered under this program, 7356.002, include inspection of any facility that does not have a specific program:**

	PAC	Type	Subject
Industry codes:	56002	Full	Drug Process Inspections (DPI)
	56002H	Abbreviated	Drug Process Inspections (DPI)

Quality Policy Activities in 2018: *Just Posted*

Category	Title	Type	Date
Pharmaceutical Quality/CMC	Liposome Drug Products: Chemistry, Manufacturing, and Controls; Human Pharmacokinetics and Bioavailability; and Labeling Documentation (PDF - 120KB)	Final Guidance	04/04/18
Pharmaceutical Quality/CMC	Regulatory Classification of Pharmaceutical Co-Crystals (PDF - 87KB)	Revised Final Guidance	02/14/18

Category	Title	Type	Date
International Council on Harmonisation - Quality	Q11 Development and Manufacture of Drug Substances--Questions and Answers (Chemical Entities and Biotechnological/Biological Entities) (PDF - 843KB)	Final Guidance	02/23/18

Quality Policies *Scheduled to Post (?)* in 2018

- **Guidance (selected)**
  - Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products—Quality Considerations [final]
  - CGMP **Interim** Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act [draft]
  - Quality Attribute Considerations for Chewable Tablets [final]
  - Data Integrity and Compliance with CGMP [final]
  - Product Development and Quality Control of Transdermal and Related Delivery Systems [draft]
  - Quality Considerations for Continuous Manufacturing (CM) [draft]
  - Using the Inactive Ingredient Database [draft]
  - Field Alert Report Submission [draft]

Quality Policies *Scheduled to Post (?)* in 2018 (cont.)

- **Compliance Programs**
  - Post-Approval Inspections
  - Inspections of Licensed Biological Therapeutic Drug Products

Quality Policy Priorities

- ✓ Patient-focused quality standards, esp. specs
- ✓ Reducing post-market submission requirements
- ✓ Fulfilling user fee commitments
- ✓ Clarifying establishment/facility identification expectations
- ✓ Guidance on complex product quality
  - Quality expectations overall, rather than just what we want to see in a submission

What it means when…

- Guidance title indicates or not **"… for Industry and FDA Staff"**
  - Good Guidance Practice regulations says guidance applies to all agency staff (21 CFR 10.115)
- Guidance cover page indicates ORA involvement or not
  - as above
-

Category	Title	Type	Date
Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products	Current Good Manufacturing Practice Requirements for Combination Products		01/10/17

Communication and Engagement: Web Site Updates

U.S. Department of Health and Human Services

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Drugs

Home > Drugs > Development & Approval Process (Drugs) > Manufacturing

Manufacturing

- Current Good Manufacturing Practice (CGMP) Regulations
- Guidances and Manuals on Pharmaceutical Quality
- Q&A on CGMPs
- Inspection/Enforcement Resources

Pharmaceutical Quality Resources

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

Pharmaceutical quality is the foundation that allows patients and consumers to have confidence in the safety and effectiveness of their medications. CDER developed a Quality Initiative and established the Office of Pharmaceutical Quality (OPQ) to ensure a uniform drug quality program across all sites of manufacture, whether domestic or foreign, and across all human drug product areas – new drugs and biologics, generics, and biosimilars—and also over-the-counter drugs and compounded drug products. This white paper provides additional background regarding OPQ and the FDA's oversight of pharmaceutical quality.

Patients and consumers can learn more about quality and how Current Good Manufacturing Practices (CGMPs) impact them.

The resources below offer information on pharmaceutical quality topics for manufacturers and applicants.

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Latest News:

- OPQ issued a **white paper** describing key considerations for applicants when preparing a Quality Overall Summary (QOS). The QOS is a summary of all quality-related information provided by applicants to regulators in drug marketing or licensing applications, including New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), and Biologics License Applications (BLAs) in the United States.
- Elemental Impurities: As of January 1, 2018, all new NDAs and ANDAs are required to meet applicable USP and ICH Q3D requirements regarding elemental impurities. **Click here** for more information.

Quality Information for Applicants: Chemistry, Manufacturing, and Controls (NDA, ANDA, BLA, and IND applications)

Quality Information for Manufacturers: Current Good Manufacturing Practices

Advancing Product Quality

FDA Presentations on Pharmaceutical Quality Topics

Contact for Further Information:

CDER-OPQ-Inquiries@fda.hhs.gov

Q&A on CGMPs

As part of the Current Good Manufacturing Practices (CGMP) initiative announced in August of 2002, and to help FDA be more transparent with CGMP policy, we have developed this question and answer resource on current good manufacturing practices. We intend to use this format to provide timely answers to questions about the meaning and application of CGMPs for human, animal, and biological drugs, and to share these widely. These questions and answers clarify statements of existing requirements or policy that are minor in nature, and as such, are considered Level 2 guidance. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-6821 (see the instructions for submitting comments in the docket). This resource is being cosponsored by CDER, CVM, CBER, and ORA. The Q&As generally clarify the existing CGMP regulations for finished pharmaceuticals: 21 CFR part 211

Questions and Answers on Specific Topics:

- General Provisions
- Organization and Personnel
- Buildings and Facilities
- Equipment
- Control of Components and Drug Product Containers and Closures
- Production and Process Controls
- Packaging and Labeling Control
- Holding and Distribution
- Laboratory Controls
- Records and Reports
- Returned and Salvaged Drug Products

Contact for Further Information:

CDER-OPQ-Inquiries@fda.hhs.gov

Strengthen partnerships and engage stakeholders

External Collaboration

- U.S. Pharmacopeial Convention (USP)
- ASTM International (ASTM)
- The Pharmaceutical Research and Manufacturers of America (PhRMA)
- Association for Accessible Medicines (AAM) [formerly Generic Pharmaceutical Association (GPhA)]
- Biotechnology Industry Organization (BIO)
- International Pharmaceutical Excipients Council (IPEC)
- American Association of Pharmaceutical Scientists (AAPS)
- International Society for Pharmaceutical Engineering (ISPE)
- Parenteral Drug Association (PDA)
- Personal Care Products Council (PCPC)
- Product Quality Research Institute (PQRI)
- US National Institute of Standards and Technology (NIST)
- Bulk Pharmaceutical Task Force (BPTF)
- Drug Information Association (DIA)
- Pharma and Biopharma Outsourcing Association (PBOA)
- International Forum on Process Analytical Chemistry (IFPAC)

CDER's Current Standards Engagement

- **USP**
  - USP Committees
    - **Chemical Medicines**
    - **Nomenclature and Labeling**
    - **Compounding**
    - **Excipients**
    - **General Chapters (Chemical & Physical Analysis, Dosage Forms, Statistics, Microbiology, Packaging, Storage and Distribution)**
  - Harmonization between USP, EP, JP through the Pharmacopeial Discussion Group
- **ASTM E55** Manufacturing of Pharmaceutical and Biopharmaceutical Products, **D10** Packaging, **E11** Statistics, **56** Nanotechnology
- **ISO Activities** - Combination Product Standards (pre-filled syringes, device change management), **ISO TC 229** Nanotechnologies**, ISO TC 217 WG 7** (sunscreens)

FDA-USP Collaboration

- In 2017 FDA (CDER, CBER, CDRH, CVM, CFSAN) had 135 liaisons to USP Expert Committees and Expert Panels
- FDA and USP management hold quarterly meetings to discuss direction and provide bidirectional feedback
- FDA supports monograph modernization, including updates to OTC monographs
- FDA-USP-CHPA roundtable in September 2017
  - Brainstormed various potential approaches to developing USP quality standards for non-application OTC products
  - Working with OND, OC, and ORA to achieve consensus on regulatory issues

Expanding Use of Voluntary Consensus Standards

- Development of a CDER informal standards recognition program is under consideration
- Benefits to FDA and Industry would include:
  - Providing industry with useful reference materials/guidance
  - Review effort can be more focused
- Promotes transparency/accountability in the development of standards
- Complements OPQ's other policy development efforts

Proposed Approach for CDER

- Publish Notice of Intent re: 'Informal' recognition/non-binding standards program
- Publish guidance on details of the program
  - Different from CDRH standards recognition program, which was created as a result of FDAMA of 1997
- Allow anyone (internal or external) to propose/submit a standard for recognition with relevant information
- Ability to informally recognize a standard in whole or in part
- CDER would develop a mechanism to review and publish 'Information Sheet' on website describing scope and other relevant information for each recognized standard

International Harmonization Efforts

- International Collaboration Initiative
  - Identify best practices in foreign regulatory agencies to enhance efficiency of our assessment processes based on visits with:
    - Australian Therapeutic Goods Administration (TGA)
    - Japan's Pharmaceutical and Medical Device Administration (PMDA)
    - European Medicines Agency (EMA)
    - Health Canada
- PIC/S
  - Development of aide memoires to harmonize inspections; participation on expert circles and training efforts
  - Relationships with many regulators; sharing of timely quality information (e.g., product quality defects, recalls)
  - USFDA hosting PIC/S Annual Seminar in Chicago, September 2018
- ICH
  - Q12 "Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management"
  - M9 "Biopharmaceutics Classification Based Biowaivers"

Mutual Recognition Agreement with EU

- Purpose:
  - Facilitate “exchange of official GMPs documents” and “reliance on the factual findings....”
  - “Facilitate trade and benefit public health” by being more efficient at inspections
- Initial focus on domestic surveillance inspections
- Implementation began Nov. 1, 2017 with
  - EU completed assessment of FDA and
  - FDA completed assessments of 8 MS Inspectorates: **Austria, Croatia, France, Italy, Malta, Spain, Sweden, United Kingdom**
  - By March 1, 2018 FDA completed 4 more: **Greece, Hungary, Czech Republic, Romania**
- Includes the vast majority of drugs
  - Most CDER-covered products (i.e., those we mutually recognize as a pharmaceutical)
- Certain products will be evaluated for inclusion in the future, such as vaccines and veterinary products
- Either party may ask the other to perform an inspection
- May disclose confidential information from inspection with other inspectorate

In Closing…

OPQ is...

Committed to:

- Patient-focused quality standards
- Strengthening our internal and external collaborations to better assure the availability of quality drugs
- Ongoing participation in global harmonization efforts to reduce barriers to innovation and continual improvement in manufacturing
- Encouraging our stakeholders to join FDA in a commitment to quality


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