



# PEPFAR

U.S. President's Emergency Plan for AIDS Relief



# Drug Product Quality Assessment Considerations Under PEPFAR

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# Drug Product Quality Assessment Considerations Under PEPFAR

## Overview –

- Differences in Standards between US Drug Product and PEPFAR Drug Product Quality Assessments (DPQAs)
- Overcoming the early challenges to performing PEPFAR DPQAs
- How assessment practices have evolved during the PEPFAR *and* GDUFA\*
- Current areas of focus for PEPFAR both pre- and post-Tentative Approval

{\* Generic Drug User Fee Acts; 2012, 2017, 2022}

# A *Quick View* of Drug Product Quality Considerations for all FDA-Approved Drugs for the US Market

**Patient-centric** (Our focus is always on benefit/risk to the patients)

- Looking for Acceptable and Reproducible Drug Product Quality
- Submission Requirements for Assessment of Drug Product Quality
  - Demonstration of Product Knowledge and Understanding (K&U)
  - Data Provided to Support that K&U
    - Raw Materials, Processes, and Facilities
    - Batch Release, Stability Studies and Validated Methods



# Drug Product Quality considerations for **PEPFAR** FDA Tentatively-Approved Drugs

**Patient-Centric** (Our focus is always benefit/risk to the patients)

- Looking for Acceptable and Reproducible Drug Product Quality
- Submission Requirements for Assessment of Drug Product Quality
  - Demonstration of Product Knowledge and Understanding
    - Data Provided to Support that Knowledge and Understanding
      - Raw Materials, Processes, and Facilities
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# ***One Specific Difference*** in Drug Product Quality considerations for PEPFAR FDA Tentatively-Approved Drugs vs. FDA Approved Drug for the US Market

## DP Storage Temperatures:

USA: ICH Zones I and II (25°C/60%RH)

PEPFAR: ICH Zones III and IV (30°C/75%RH)



**NOTE:** We (FDA) need assurance that product quality will be maintained for the medicine under storage conditions that the medicine will encounter in the patient's home.

# Challenges for Drug Product Quality Assessments PEPFAR Drugs during early days of PEPFAR

## Time Constraints

Urgency in Early Days was Severe due to Minimal Number of Medications Available



## FDA Resource Constraints

Limited Scientific Staff Prior to GDUFA;  
The Single Scientist Assessment Approach



# How FDA overcame these challenges for Drug Product Quality Assessments Drugs

## Time Constraints

Urgency in Early Days was Severe due to Minimal Number of Medications Available

- **Less Data at Filing with solicited updates (amendments)**



## FDA Resource Constraints

Limited Scientific Staff Prior to GDUFA

- **Prioritization**
- Single Scientist Assessment Approach
- **Delegation/Split Assessments**



# Changes in PEPFAR ANDA Assessments compared with the current OPQ Aligned Team approach under GDUFA

## Early PEPFAR / Pre-GDUFA

Single assessor process

Prioritization, no formal goal dates

Resource limited (backlog)

## Current PEPFAR / GDUFA

Team-based assessment approach\*

Established Assessment Goal Dates\*\*

Resources greatly enhanced (no backlog)

\* **OPQ Aligned Team** -Drug Substance, Drug Product, Manufacturing Process, Biopharmaceutics, Project Manager

\*\* PEPFAR Prioritization still exists under GDUFA



# *Current Priorities* for PEPFAR Drug Product Quality Assessment – Reaching Tentative Approval



We continue to move PEPFAR ANDAs toward **Tentative Approval Status**

- Focus on “Combo” products – contain more than one active pharmaceutical ingredient
  - Increased complexity
    - potential interactions between actives and/or excipients
    - impurity/degradant issues

Atazanavir Sulfate / Ritonavir Tabs  
Lamivudine, Zidovudine, Nevirapine Tabs

Lopinavir / Ritonavir Tabs

Efavirenz, Lamivudine, Tenofovir Disoproxil Fumarate Tabs

Lamivudine / Zidovudine Tabs  
Dolutegravir, Emtricitabine, Tenofovir Alafenamide Tabs

## Current Priorities for PEPFAR Drug Product Quality Assessment – Post Tentative Approval

*Maintaining* Tentative Approval Status when *Minor Changes* are made

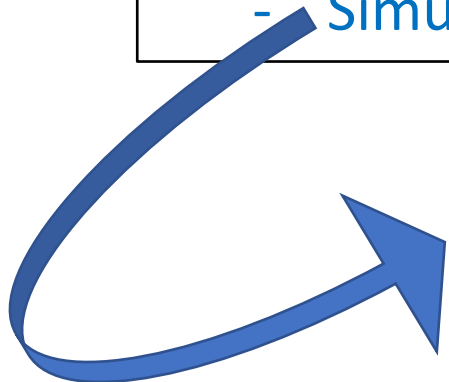
- Increasing drug product shelf life, typically beyond 24 months
- Increasing tablet count per bottle to minimize visits to doctor/pharmacist
  - Typically, 3-month (90 tablets/bottle) or 4-month (120 tablets/bottle) dosing

**NOTE:** For both cases above, we need assurance that product quality will be maintained for the patient.

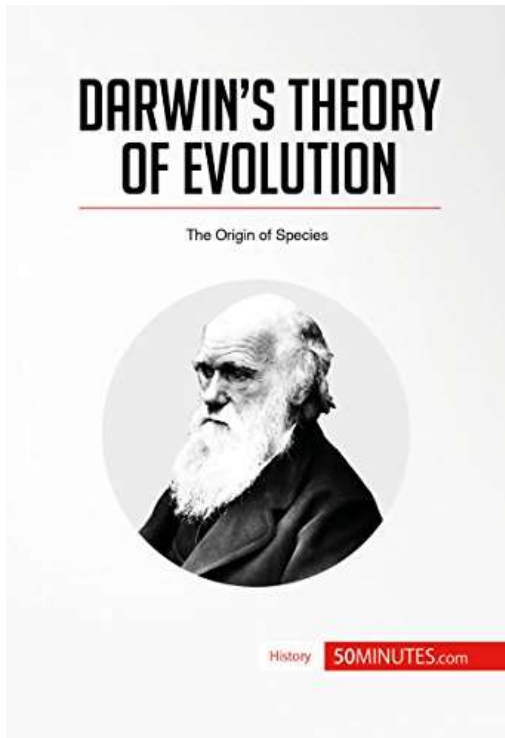
# Current Priorities for PEPFAR Drug Product Quality Assessment – Post Tentative Approval

**Maintaining** Tentative Approval status when **Minor** changes are made

- Increasing drug product shelf life, often beyond 24 months
  - Additional stability data provided for assessment
- Increasing tablet count per bottle to minimize visits to doctor/pharmacist
  - Simulated “In-Use” Studies

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- Repeated opening/closing of the bottle on a daily-basis with removal and testing of tablets to confirm that critical quality attributes are maintained under these conditions.

# Summary of Drug Product Quality Assessment Considerations Under PEPFAR



We continue to adapt to urgent assessment needs, like the PEPFAR program, by improving our time to reach a decision on drug product quality...

*...without compromising our quality standards that support that important, patient-centric decision.*

