aam
Association for Accessible Medicines

Biosimilars Council
A Division of the Association for Accessible Medicines

GRx+Biosims™
Generic + Biosimilar Medicines Conference

Essential Performance Requirements Demystified

Henri Akouka, P.E.
Associate Director, R&D, Teva Pharmaceuticals

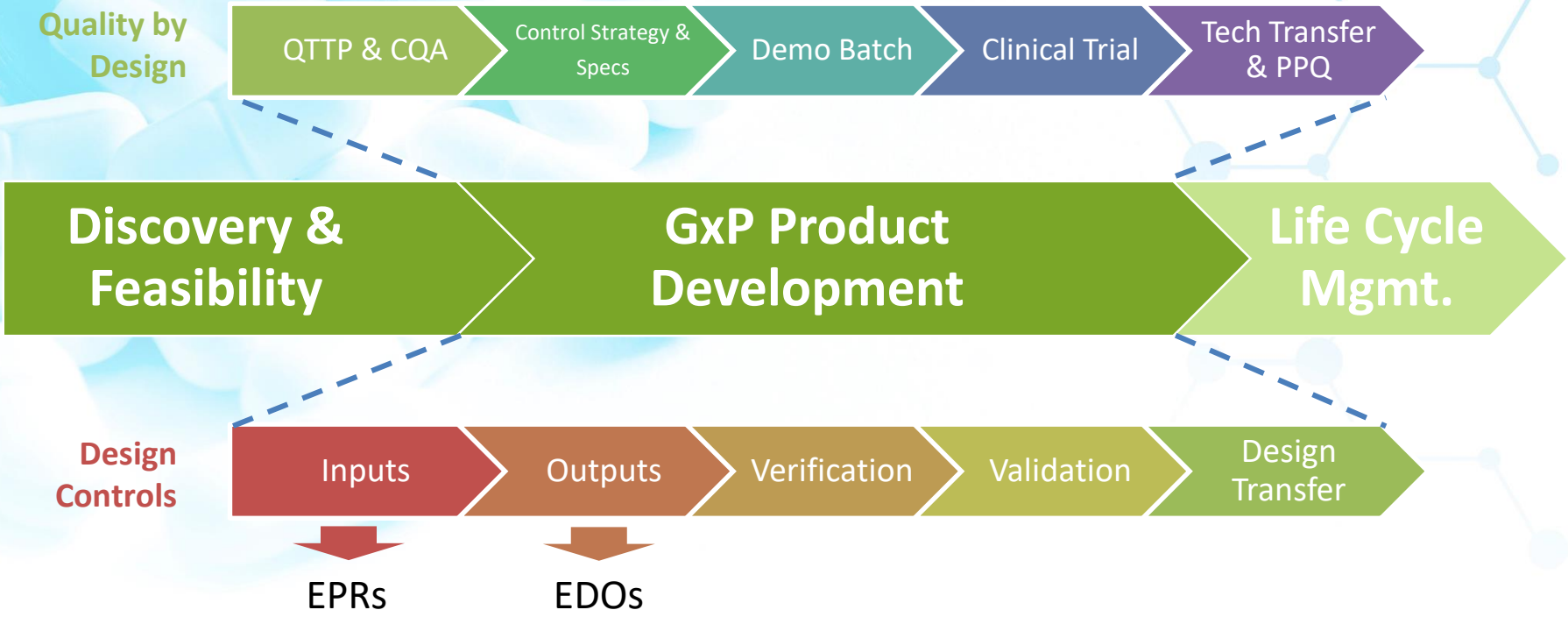
Disclaimer

The views expressed in this presentation are those of the presenter and do not necessarily reflect the views of Teva Branded Pharmaceutical Products R&D, Inc. or any of its corporate affiliates.

Agenda

- Combination Product development overview
- What are Essential Performance Requirements and Essential Design Outputs?
- How do we determine them?
- What do we do with them?

Combination Product Development



EPRs and EDOs - Where do I start?

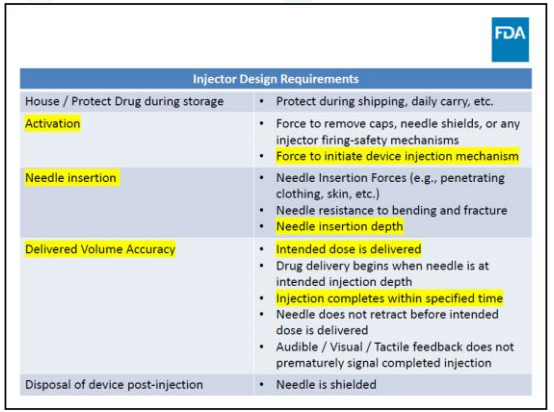
- Are you developing your Combination Product under Design Controls?
- Are you performing Risk Management on your Combination Product?
- You’re 95% of the way there

Essential Performance Requirements (IEC 60601-1:2005)

- Performance of a clinical function, other than that related to basic safety, where loss or degradation beyond the limits specified by the manufacturer results in an **unacceptable risk**.
- "Note that it is possible to have a medical device with no Essential Performance Requirements. What that means is that the device risks are controlled in such a way that the loss or degradation of any of its clinical functions do not result in unacceptable risk." *Safety Risk Management for Medical Devices: Elahi, B. (2018)*
- What about Efficacy?
  - Life Saving Treatment – Delivered Volume IS an EPR
  - Non-Life Saving Treatment – Delivered Volume is NOT an EPR

Essential Performance Requirements (FDA)

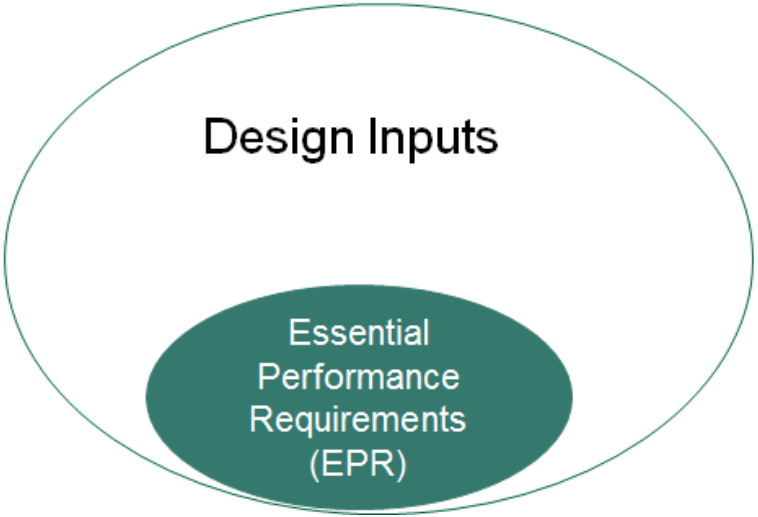
- "We are focused on device clinical performance at the time of use" - *CAPT Alan M. Stevens*
- What about Safety?
  - Life Saving Treatment – Cap Removal Force IS an EPR
  - Non-Life Saving Treatment – Cap Removal Force is NOT an EPR
- Other FDA examples for an Autoinjector
  - Activation Force
  - Needle insertion depth
  - Delivered Volume
  - Injection Time



Injector Design Requirements	
House / Protect Drug during storage	• Protect during shipping, daily carry, etc.
Activation	• Force to remove caps, needle shields, or any injector firing-safety mechanisms • Force to initiate device injection mechanism
Needle insertion	• Needle Insertion Forces (e.g., penetrating clothing, skin, etc.) • Needle resistance to bending and fracture • Needle insertion depth
Delivered Volume Accuracy	• Intended dose is delivered • Drug delivery begins when needle is at intended injection depth • Injection completes within specified time • Needle does not retract before intended dose is delivered • Audible / Visual / Tactile feedback does not prematurely signal completed injection
Disposal of device post-injection	• Needle is shielded

Essential Performance Requirements (Proposed)

- EPRs are the subset of Design Inputs that impact safety or clinical performance at the time of use by the patient or user.
- We don't submit our Design History File and Risk Management File to CDER and CBER so we need an executive summary in our submission!



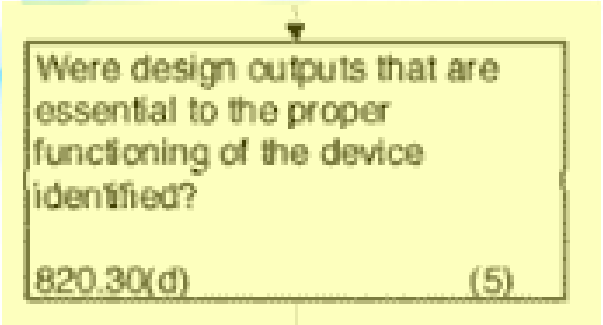
What about Essential Design Outputs?

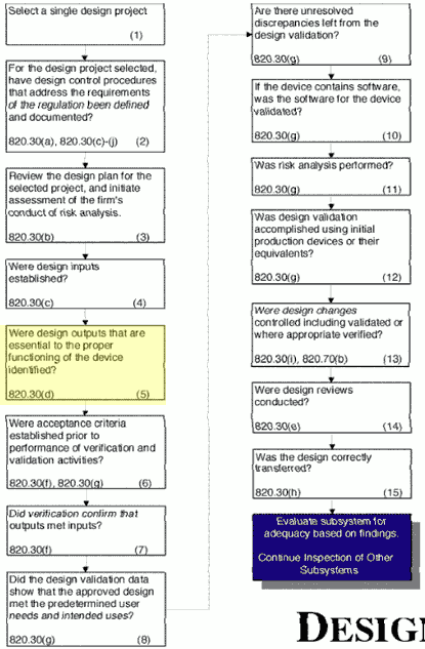
- Essential Design Output (FDA) – Design Outputs that are essential for the proper functioning of the device.
- Are there Design Outputs that aren't essential?
- Essential Design Output (proposed) – Design Output that traces to at least one EPR in the Trace Matrix is an EDO

FDA Inspection Guide (Design Controls)

Inspectional Objectives

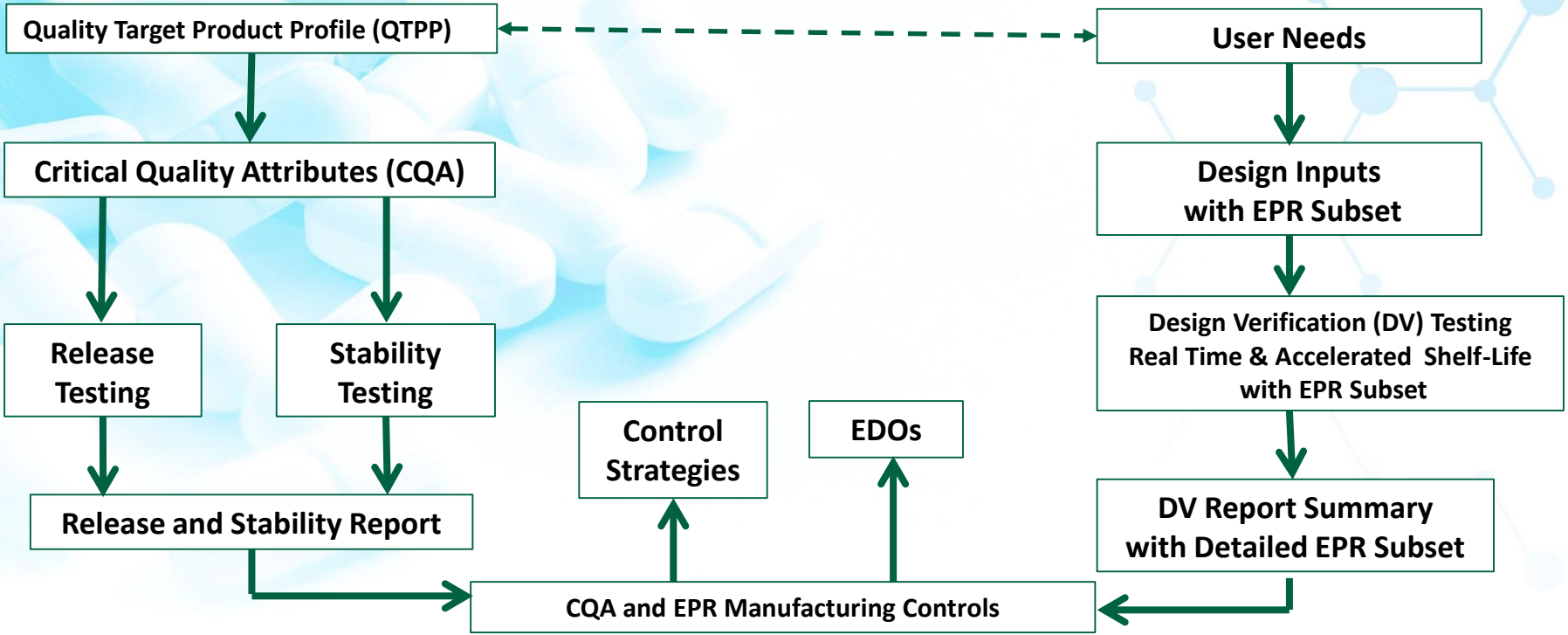
- "5.Verify that the design outputs that are essential for the proper functioning of the device were identified."





DESIGN CONTROLS DECISION FLOW CHART

CQAs and EPRs/EDOs in CP Development



Summary

- EPRs and EDOs come from your Design Control and Risk Management Process
- EPRs and their controls should be clearly specified in your submission
  - NDA, ANDA, and BLA submission formats are not intuitively set up for Combination Product submissions.
  - Pick a section for EPRs and their controls and draw attention to it
  - FDA will be looking for analogous Drug Product information in 3.2.P.2 Pharmaceutical Development Report
- EDOs and their controls should be available during inspections
  - Have your Trace Matrix ready with your EDOs and their controls highlighted