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Writing CERs to Rev. 4: Points to Consider and Gaps to Bridge

Mary Beth Henderson, Ph.D., MBA

May 23, 2017

Thank you for joining us!

We will begin at Noon Central Time.

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Your phone line has been muted.

Type in any questions you have in the Questions box

and we'll have Q&A at the end of the presentation.

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Agenda

- Background
- Suggested Considerations
  - Quality Plan
  - Update SOPs and Templates
  - Update Job Descriptions
  - Align Labeling
  - Align Risk File
- Gaps to Bridge
  - CER Plan
  - Search Strategies
  - Equivalence
  - State of the Art
  - Pro-active PMCF
- Summary

Background

CERs

Required Elements

- Demonstrate
  - Compliance with Essential Requirements
  - Device is safe
  - Performs as intended
  - Known and foreseeable risks and AEs minimized and acceptable when weighed against benefits
- Claims supported by evidence
- Device state-of-the-art

CERs

Definition:

"**Clinical Evaluation**" means the assessment and analysis of a ***systematic*** and ***planned*** process to continuously generate, collect, analyze and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer.

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (1).

CERs

Definition:

"**Clinical Data**" means information concerning ***safety*** or ***performance*** that is generated from the use of a device and is sourced from the following:

- clinical investigation(s) of the device concerned,
- clinical investigation(s) or other studies reported in scientific literature, of a device for which ***equivalence*** to the device in question can be demonstrated,
- reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated,
- clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up.

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (1)

Suggested Considerations

Develop a Quality Plan for CERs

Create a document which includes:

- Plan to meet Rev. 4 requirements and timing, including any potential updates for the MDR
- Updated SOPs/Templates
- Approaches to PMCF

Discuss with NB either pro-actively or during audit

Identify and obtain resources necessary to meet your timelines

Update SOPs and Templates

- At a minimum update your SOP to incorporate the new requirements called out in Rev. 4
- May want to consider a high-level SOP for CER production and another for CER Plans and/or literature search protocols
- May be a good time to revise CER template to follow the recommended template in *Annex 9. Clinical evaluation report – proposed table of contents, examples of contents*
- May want to incorporate CER checklist (*Annex 10. Proposed checklist for the release of the clinical evaluation report*) into your SOP
- Don't forget to address new requirements for CER updates and Declaration of Interest

Update Job Descriptions

- Need to identify who will be involved in preparing CERs
- Need to address and define qualifications and training for those involved in preparing CERs

Update Job Descriptions

- Define and document qualifications
- In general evaluators should have:
  - Research methodology
  - Device technology and clinical use
  - Training and experience
    - “a degree from higher education in the respective field and five years of document professional experience; or
    - 10 years of documented professional experience if a degree is not a prerequisite for a given task.”

Align Labeling

Ensure consistency across all labelling documents for the products within the scope of the CER

- Indications for Use
- Contraindications
- Precautions
- Warnings

Align Risk File

- Ensure consistency across the various risk documents in types of identified risks and harms and their mitigations
- Align risk analyses with label claims
- Consider any changes/updates required to meet ISO 14971:2016 requirement

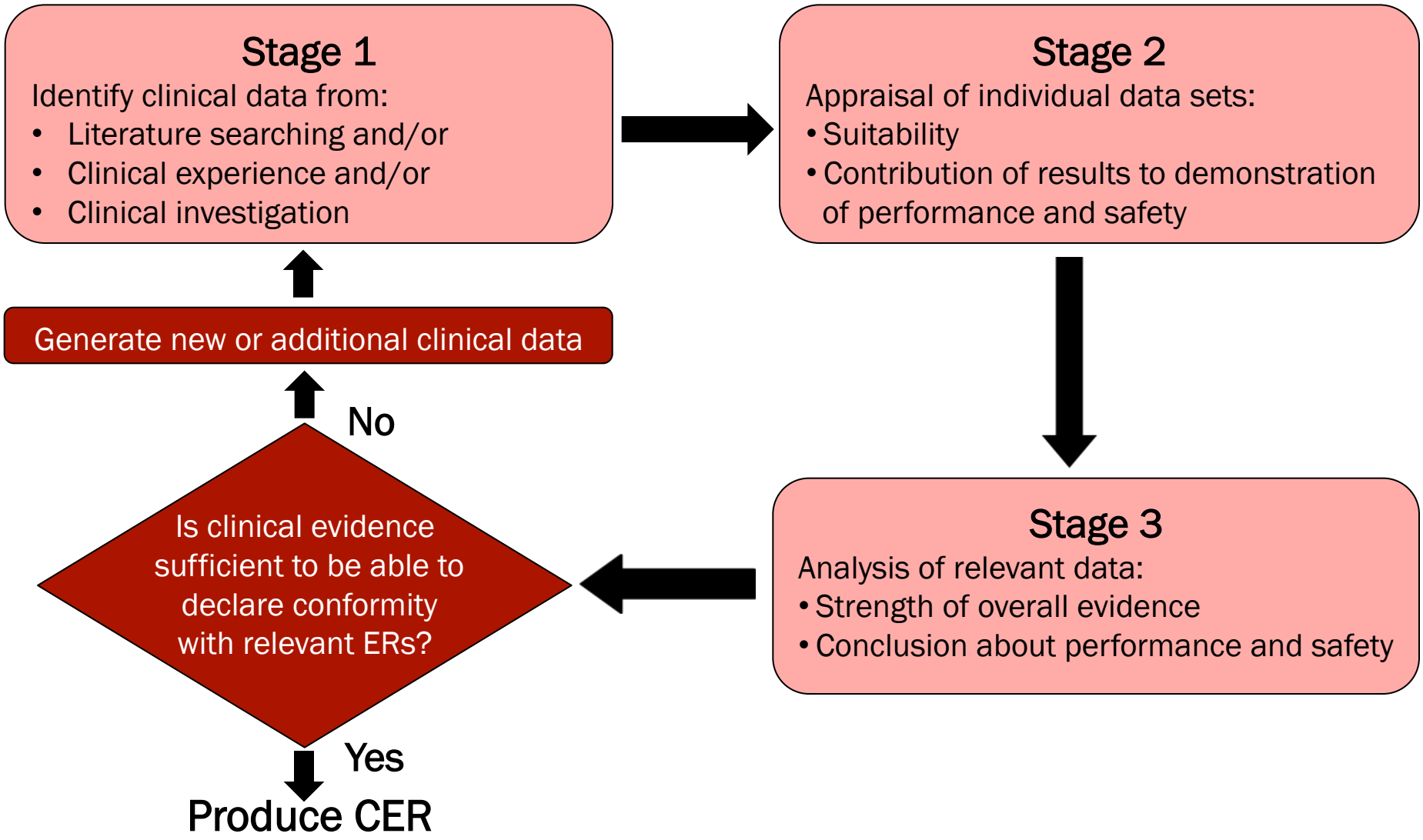
Gaps to Bridge

CER Plan

Resources for CER Preparation:

- Regulatory
- R&D (Design inputs/specs)
- Labeling
- Preclinical
- Clinical PMS/PMCF
- Risk Management
- Library Sciences
- Clinical (medical) expertise

CER Plan

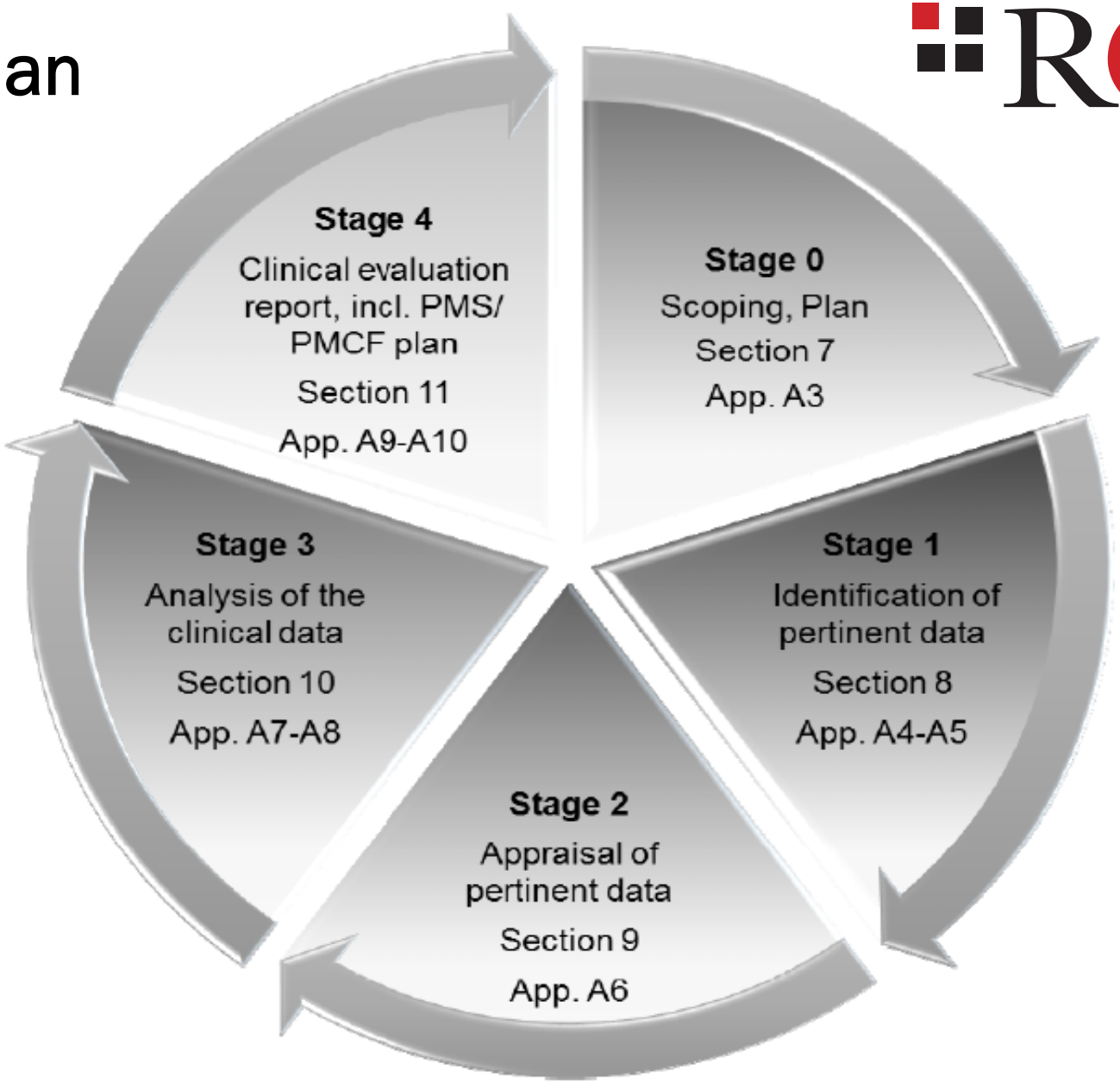


CER Plan

Stages of CER Preparation:

- Stage 0 Define Scope and Plan
- Stage 1 Identify Data requirements
- Stage 2 Appraise available data
- Stage 4 Analyze and conclude
- Stage 5 Finalize

CER Plan



CER Plan

Aspects to Consider for Plan:

- Device description, including areas that require specific attention
- Time frame (for updates)
- Questions of equivalence
- Risk management documents
- State of the Art
- Data Sources
- Device Changes
- Clinical Concerns
- Post-Market Surveillance Data
- Post-Market Clinical Follow-up

Search Strategies

New:

- Specific need to search multiple databases
  - EMBASE
  - Cochrane CENTRAL trails register
- Internet searches
- SOA searches

Search Strategies

Continued:

- Identify search methodology
- Justify sources
- Set search terms
- Set search dates
- Set inclusion/exclusion criteria
- Set analysis criteria

Equivalence

New-ish:

- Must demonstrate equivalence to a single device(s)
- Provide clinically relevant specs, properties in comparison table

New

- Manufacture is expected to have non-clinical information regarding the equivalent device
- Equivalent device must be CE-marked and used in accordance with its intended purpose (can be excepted with appropriate justification)

Equivalence

What does this mean for the writer?

- Establishing equivalence has become more difficult
- May limit equivalent devices to previously CE-Marked earlier models
- Devices tested against “predicate” devices may provide sufficient “pre-clinical” data to justify equivalence (update)
- This may be an area where standards can be leveraged
- Use of equivalents will be severely limited

State of the Art

SOA based on:

- Standards
- Guidance documents
- Info relating to the medical condition
- Benchmark devices
- Other devices and medical alternatives available to target population

State of the Art

SOA:

- Describes the clinical background and identifies the current knowledge
- Identifies potential clinical hazards
- Justifies the validity of criteria used for demonstration of equivalence (if appropriate)
- Justifies surrogate endpoints (if appropriate)

State of the Art

SOA should address:

- Clinical Background
  - Clinical condition
  - Prevalence of condition
  - Natural course of the condition
- Other Devices/Medical Alternatives
  - Target population
  - Historical treatments
  - Available medical options
  - Existing/benchmark devices

State of the Art

What does that mean for the writer?

- Literature review
  - Consider risk/benefit
  - Deficiencies with other approaches
  - Does subject device address a gap?
  - If not, is the benefit/risk profile comparable
- Focus on current SOA
- Keep SOA high level, based on device indications for use and alternative therapies

Pro-active PMCF

Pro-active PMCF

- Customer surveys
- PM trial with targeted patient populations
- Surveillance trials
- Registries
- Expert User Groups
- Long-term follow up of pivotal patients
- Case studies

Summary

Rev. 4 Summary

- Rev. 4 is more prescriptive and will need to be aligned with MDR (stay tuned)
- Medical device companies need to develop a plan to update CERs for compliance and discuss with NB
- Don’t be afraid to think outside the box – we’re all looking for appropriate (justifiable) approaches to meeting the new requirements
- Don’t be afraid to question your NB should their interpretation of the requirements not match yours

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Questions

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