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Topics:

- Various Core Labeling used during Clinical Development and their interrelationships
- How early to start and how and when to transition to core labeling for a development product
- Benefits of applying the principles of core labeling during clinical development
“The CIOMS Working Group V proposes that the IB contain a section identical in structure to the Company Core Safety Information that is included in the Company Core Data Sheet for a marketed product, and that it be referred to as the Development Core Safety Information (DCSI). This would satisfy the need to help investigators and sponsors more effectively by presenting and updating a focused, dedicated Development Core Safety Information section that can conveniently be placed within the IB, perhaps as an Appendix. Furthermore, it is proposed that the DCSI develop into the CCSI that is included in the first Company Core Data Sheet for the product's entry into the market.”

[CIOMS working group V]

During drug development, companies may have a variety of labeling related tools to

• Facilitate drug development with target labeling in mind
• Align desired marketing and labeling objectives with development program design (study design)

Examples of these labeling tools during drug development (with no standard terminology):

• Investigator Brochure (IB)
• Target Labeling (TL)/ Target Profile
• Development Core Data Sheet (DCDS)
• Development Core Safety Information (DCSI) – CIOMS V
• FDA Target Product Profile (TPP)
• Others
Types of Core Labeling during Clinical Development
- IB vs CCDS

- Investigator’s Brochure is the “Predecessor” of the CCDS
- Both IB and CCDS
  - Represent Company’s view of a product and its safety profile
  - Are internal documents shared with external persons/institutions but are not fully public
  - Are with multi-nation/region approach

Types of Core Labeling during Clinical Development
- Development Core Data Sheet (DCDS) vs Target Labeling (TL)

- DCDS (Development Core Data Sheet)
  - for development labeling
- TL (Target Labeling)/Target Profile
  - set of living objectives for the development team

Both DCDS and TL
- are internal documents
- do not follow external format requirement
Types of Core Labeling during Clinical Development – Target Product Profile (TPP) and Draft SmPC

- TPP: FDA Target Product Profile
- dSmPC: Draft SmPC

Both TPP and dSmPC
- are for discussion with Regulatory Agencies
- are based on DCDS and TL
- can follow FDA TPP format and EU SmPC format

Types of Core Labeling during Clinical Development
Development Core Safety Information (DCSI) vs Company Core Safety Information (CCSI)

DCSI contains a set of “evolving” safety information including
- Expected events
- Anticipated events
- CI, W&P etc.

CCSI contains a set of “established” safety information including
- ADRs/ IAs
- Anticipated ADRs/ IAs
- CI, W&P etc.
See presentation in session 2, “The Adverse Reactions and Interactions Section of a CCDS” for definitions of adverse event or adverse reaction and the expectedness for safety reporting and labeling.

Format and features of DCDS - example
The format of the DCDS can be customized to accommodate the specific needs for a development project. DCDS can contain, at the same time, the target and confirmed context, and anticipated local deviations.

Topics:

- Various Core Labeling used during Clinical Development and their interrelationships
- **How early to start and how and when to transition to core labeling for a development product**
- Benefits of applying the principles of core labeling during clinical development
When to start with a Development Labeling

1. Early compound
2. Phase 1
3. Phase 2
4. Phase 3
5. Study results
6. Submission

Core Labeling Team

- Pre-clinical
- Pharmacokinetics
- Toxicology
- Global Pharmacovigilance and Epidemiology
- Quality Assurance
- Clinical
- Drug Regulatory Affairs (including CMC)
- Medical Affairs and Marketing
- Legal
When to start with a development labeling

- As soon as possible, as this can be used for agency discussions.
  - US: Target Product Profile
  - EU: Draft SmPC

When to start drafting local labeling ...

At some point of time add, at least, USPI and EU SmPC
- Depends on Project team but generally 12-18 months before submission
- CCDS stays company opinion
- CCDS can be used to develop proposed USPI and EU SmPC, and keep them “in line”

TL – DCDS – CCDS Interface
Labeling Deliverables

*EOP: end of phase
From DCDS to CCDS to Local Labeling

As early as possible

Approx. 18 months

Internal approval

Submission FDA

Submission EMEA

From DCDS to CCDS to Local Labeling

Early Phase(s)

Close(r) to submission

If needed
Topics:

- Various Core Labeling used during Clinical Development and their interrelationships
- How early to start and how and when to transition to core labeling for a development product
- Benefits of applying the principles of core labeling during clinical development

Benefits of applying the principles of core labeling during clinical development:

- Promote consistency in decision making across the development and marketing phases
- Identify gaps in development plan through
  - Internal discussion
  - Interaction with HAs
- Start early that you can influence the design of phase 3 trials and their statistical analysis
- Can be used for different target claims (indications), different audiences, and for different purposes
• In addition to Core content, also prepare anticipated national deviations (content and wording), e.g., ADR section