Introduction to Core Labeling

Gerrit-Jan Nijveldt
Sr. Director Global Regulatory Affairs Labeling
SANOFI

Core labeling from 10,000 Feet

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Introduction to Core Labeling

What will be (briefly) discussed in this introduction:

- Reason to have core labeling
- What is core labeling?
- What is needed in a company (basics)
- Who is involved in the process?
- When to start?
- What do you need?
- Why do you need it?

This part will only be the introduction, further details will be discussed during the remainder of this conference.

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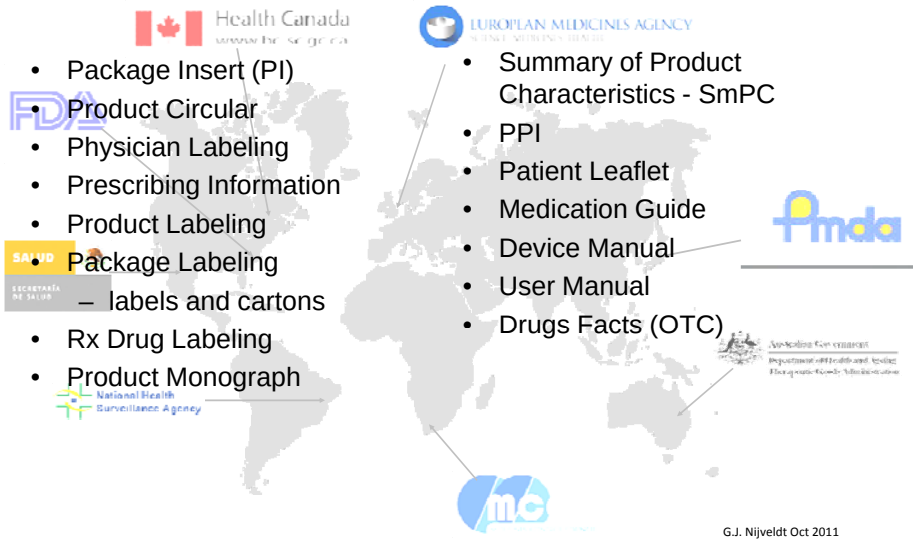
Labeling around the world – what are we dealing with?



- Package Insert (PI)
- Product Circular
- Physician Labeling
- Prescribing Information
- Product Labeling
- Package Labeling
  - labels and cartons
- Rx Drug Labeling
- Product Monograph

- Summary of Product Characteristics - SmPC
- PPI
- Patient Leaflet
- Medication Guide
- Device Manual
- User Manual
- Drugs Facts (OTC)

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Labeling – What is it?

It's the end-result of your drug development process!

- Labeling constitutes the agency-approved information on the use of the product.
- Based on the results of scientific research that demonstrate safety and efficacy in humans.
- The only document prepared in the Dossier to be publicly available.

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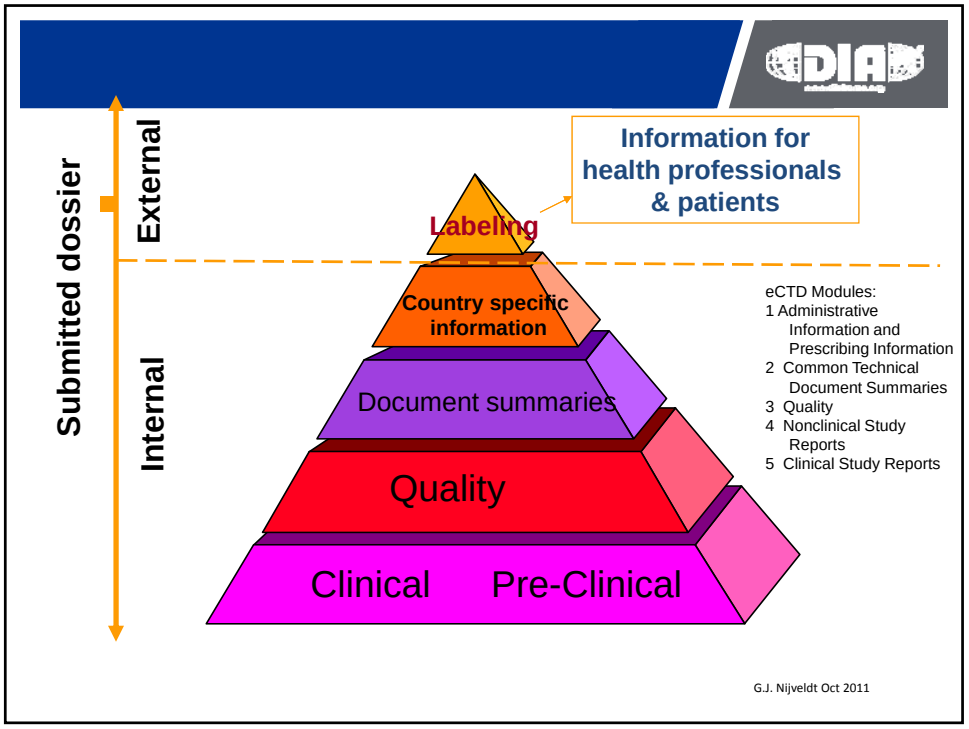

And...

- Serves as the basis for prescribing of the medication but also advertising and promotional activities (*globally*).
  - For some countries, e.g. US, any promotional claims that do not conform to approved labeling can render the product *misbranded*.

It is important for the physician and patients but also the company, so how to control the content on a global basis.

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Core Labeling – what should it be

- Represents company position based on the data and developed for the marketing authorizations worldwide
- Should *not* be a regulatory agency position
- Serves as the basis for worldwide labeling
- Updated as data become available

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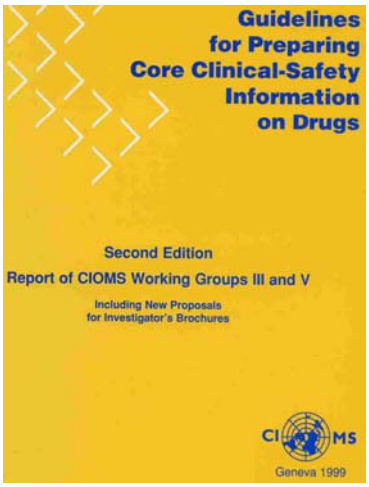
Core Labeling - basis



Sometimes seen as the starting point for the core labeling principle.

CIOMS III – 1995

Superseded by

CIOMS V - 1999

(CIOMS states that the CCDS that companies already have could be used as global reference doc. At that time, all companies represented in CIOMS already had something like CCDS.)

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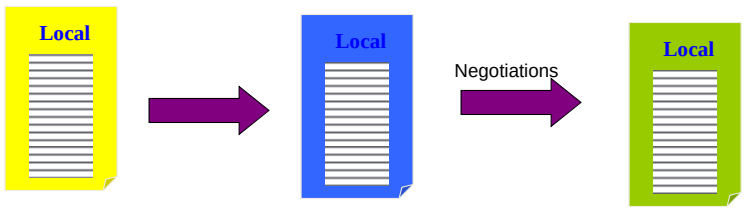
Core Labeling – Why?

Why not use a local data sheet as reference document?



Submitted by Pharmaceutical Company

Review by Regulatory Agencies

Final Outcome

Approved

Result: A Local label does not fully represent the company position, therefore not the best solution as an internal regulatory tool although there might be some reasons to do so.

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Core Labeling – Why? (2)

Real Example:

Pregnancy:

Contraindicated

Pregnancy:

Category C

Use when benefit outweighs the risk

What is the company opinion?

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Corporate Labeling

What are we talking about …

Companies may have a variety of names for Corporate labeling documents, such as:

- **Core Safety Information**
- **Core Data Sheet**
- **Worldwide Physician Circular**
- **Company Core Data Sheet**
- **Core Label**
- **Etc.**

From now on we will use the term Company Core Data Sheet (CCDS) or core labeling in this conference

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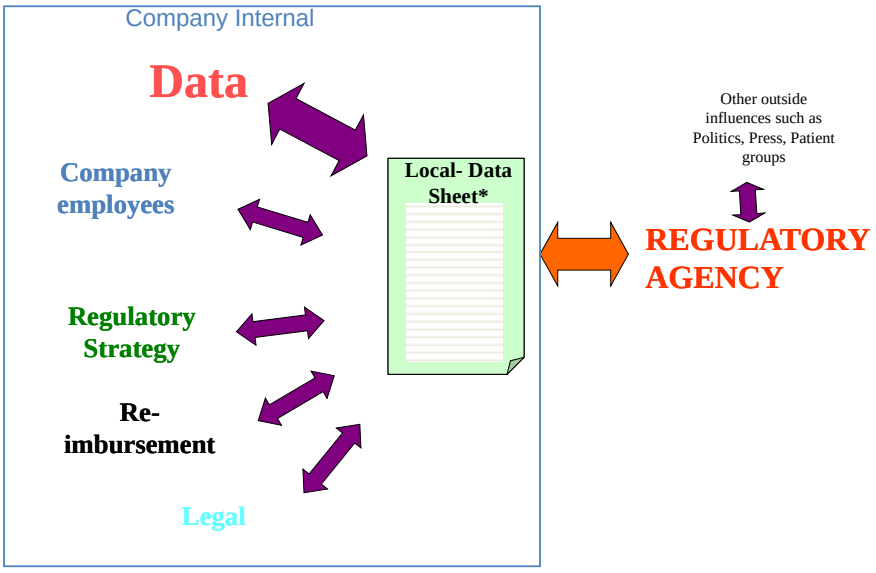
Who "creates" Local Labeling (influence)



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* e.g. SPC/PI/PM

Use for a Company Core Data Sheet (CCDS)

Harmonized labeling

Global consistent labeling for:

- **Products with ongoing Life Cycle management**
- **All marketed products**

Can also be used for products in development

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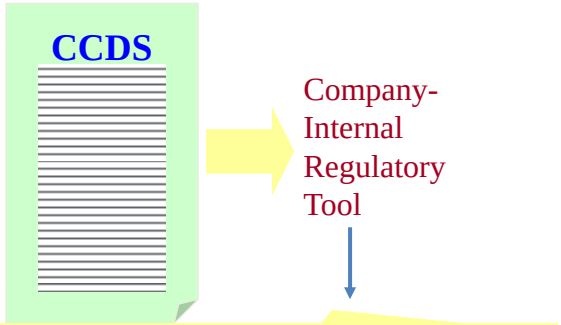
Uses of a CCDS (1)



- **Communicates Company opinion of a product to Affiliates.**
- **Possible keystone of company-internal global labeling system.**

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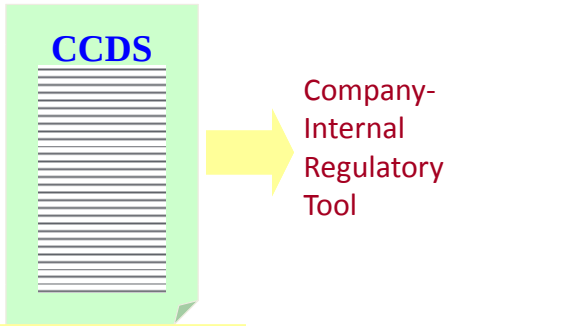
Uses of a CCDS (2)



- **Discloses company's view of safety profile to regulators.**
- **Lets regulators expect attempts to implement a certain set of safety information in their local market.**

More detail in session 5

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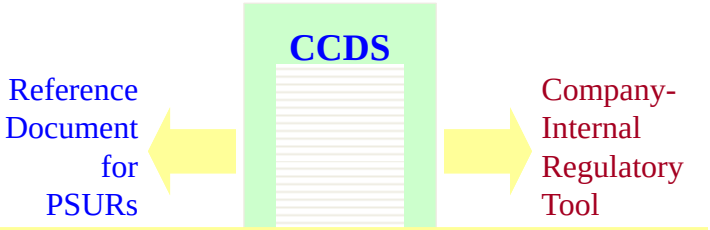
Uses of a CCDS (5)



If regulatory authorities disagree with statements in the CCDS (i.e. do not approve them for local labeling), a company can reconsider, disregard or adopt their position for the CDS.
This is also the case with addition into local labeling that are not in the CCDS

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Core Labeling

- What is included?

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Content of CCDS – Structure

This is an internal company decision, but can be based on a local format e.g.,:

- **SPC format**
- **"Old" US-PI format**
- **"New" US-PI format (PLR)**

Or use a region Neutral structure that combines different structures

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Content of CCDS – Structure

•What to include?

- Therapeutic class
- Indications
- Dosage and Administration
- Contraindications
- Warnings/Precautions
- Drug Interactions
- Pregnancy/Nursing
- Special Populations
- Adverse Reactions/Side Effects
- Overdosage

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Content of CCDS – Structure

- "Optional" sections
  - Chemistry
  - Mechanism of Action
  - Clinical Pharmacology
  - Clinical Studies
  - Animal Toxicity

Detailed content discussed in session 2 and 3

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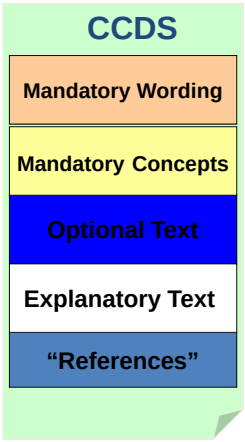
Core Labeling – content (1)

The CCDS can contain the following texts pieces or concepts. The meaning of this will support implementation



More detail at the end of this session

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Core Labeling – Implementation

Ways of communicating labeling within the company

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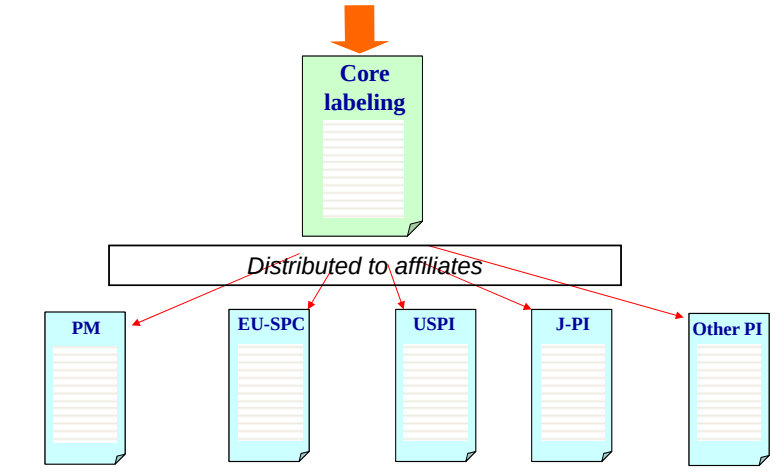
Core Labeling – Implementation

Pharmaceutical Company - HQ



Option: Local Labeling written by HQ or local affiliate

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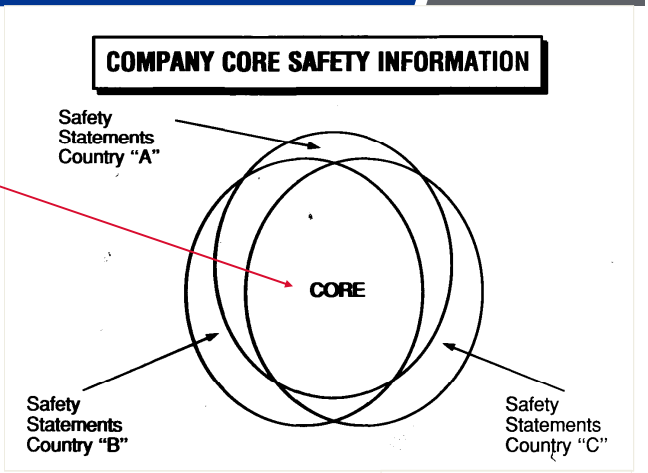
Core Labeling – Implementation

Mandatory CCDS is **actively defined by Company Headquarters.**

"Headquarters" may decide to omit some local items from CCDS.

Local labeling that is missing some CCSI items needs to be updated (at least: try)



from CIOMS III/V report

This could be used as a start for a CDS for "old" product

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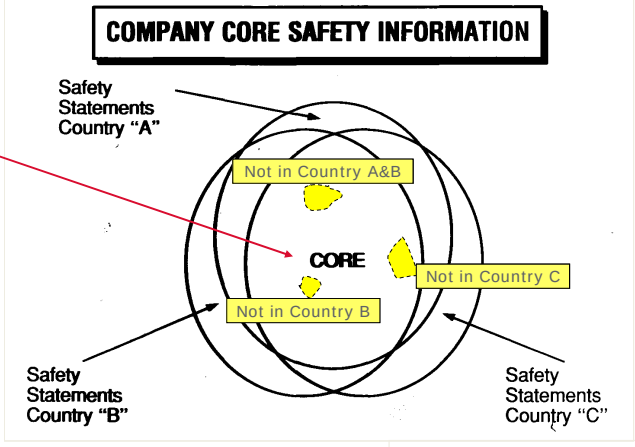

from CIOMS III/V report

Companies are not always successful in updating local safety content.

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Core Labeling

- Where (and when) do you start?

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When do you start?

- When a new chemical entity is determined to be a candidate for use in man.
- Limited pre-clinical data available
  - Chemistry
  - Pharmacology
  - Toxicology
- Before clinical trials begin or early on in development, created to enhance the development process

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Use of Core Labeling during Development

Or how core labeling can impact drug development, and how drug development can impact core labeling

Further details in session 4

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Development Labeling

During drug development …

Companies may have a variety of labeling-related tools (no standard terminology).

- **Target product profile**
- **IB**
- **Development core safety information**
- **Detailed target labeling**
- **Evolving CCDS**
- **Evolving national submission labeling**

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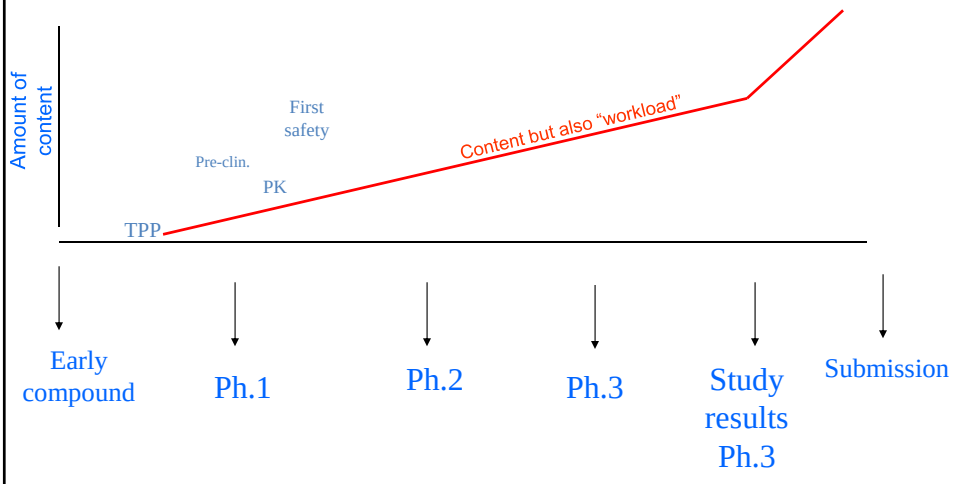
Development Labeling

When to start with a Development label …



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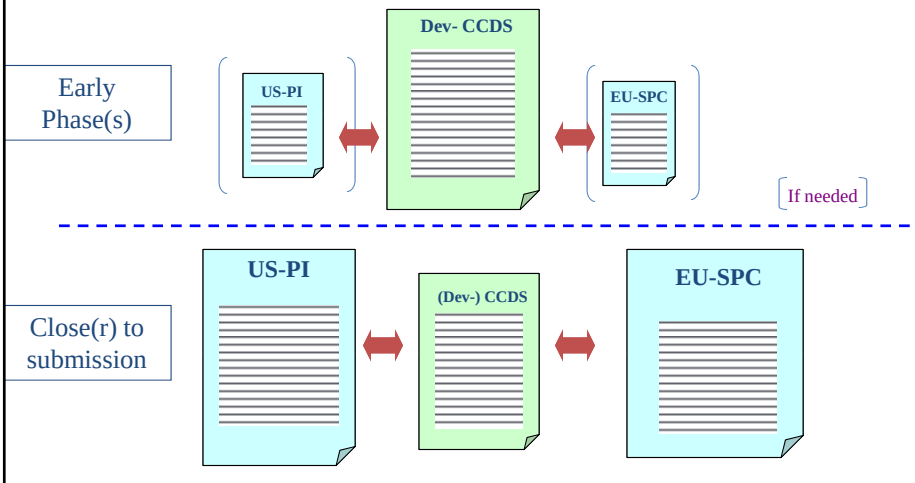
Development Labeling



This depicts the workload on the documents not the importance

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Development Labeling

When to put in place the CCDS …

There are different scenarios for this (*random order*):

1. **After first approval (labeling content has been put to the test)**
2. **After first submission (it is the company opinion)**
3. **Before submission at time of final internal approval (same time as some local data sheets are approved)**
4. **When a "Corporate" PSUR is in place**
5. **Start with Development CCDS during very early phase.**

In case of 2, 3, 4 and 5 an update to the CCDS might be needed after first approval(s).

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Core Labeling – How to support

Business Rules to get it right!

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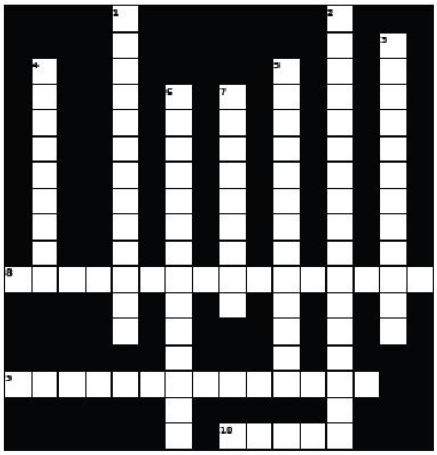
The Core Labeling crossroad



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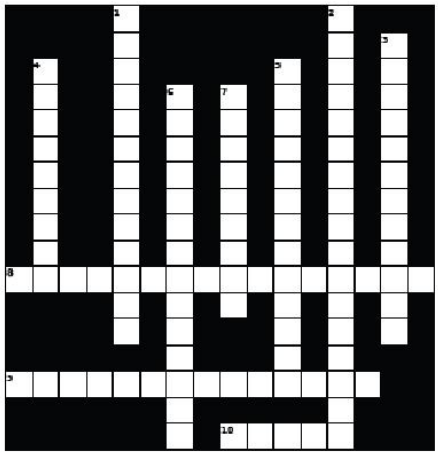
The Core Labeling crossroad



Across

8 labeling is done with a defined concept set down by authorities and/or companies
9 put action into effect
10 believing is good checking is better

Down

1 without this nothing works in a company
2 help from upper echelons
3 main building within company
4 country with a company
5 company labeling document
6 labeling document in country
7 something you must do!

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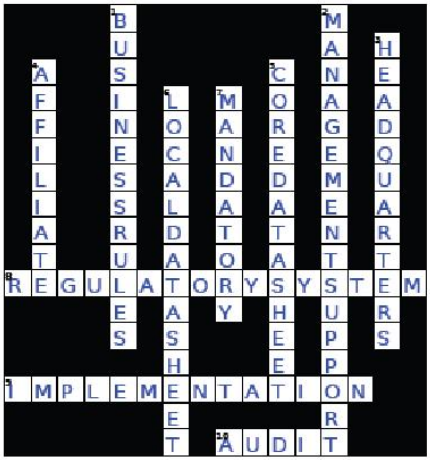
The Core Labeling solution



Now when you see this the crossword puzzle is easy

But all the "words" need to be in place for this to work

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"Business Rules"

Typically, pharmaceutical companies define an extensive set of business rules that address common questions and provide guidance. Many of these rules are in the form of SOPs and more detailed work instructions

Simplified the Business rules need to address:

1. Structure
2. Content/Terminology
3. What is mandatory to implement
4. What is the desired level of similarity between CCDS and local labeling
5. When do affiliates need to obtain HQ approval before acting l ocally

More Details in this session and session 5

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Do not forget!

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Conclusion

The Company Core Data Sheet (CCDS):

- company-internal regulatory tool
- Regulatory/Pharmacovigilance tool, for the use in PSUR
- used to achieve global company consistency in labeling
- Requires a set of business rules (ideally)
- Benefits the drug development process when used early in development

How and where to start?

- New products
- Business rules

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Conclusion (2)

Pros

- **Global consistent labeling**
- **Company document for Pharmacovigilance**
- **Company opinion looking at the data not influenced**
- **Difficult to use a local label as company document**

Cons

- **Health Authorities input ⇒ challenge to keep harmonized labeling**
- **Agencies communicate with and look to each other**
- **Extra document to create**

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Don't forget answers might come later during the two days

Enjoy the conference!

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