



**Federal Agency for Medicines and Health Products  
(FAMHP)**

**Practical implications of changes within the herbals regulatory  
environment:**

**03. Applications for HMP authorization and THMP registration:  
how?**

Unit Homeo - Phyto



# Orienting the dossier

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Applicant wants to market a herbal medicinal product  
What kind of evidence does he have?

## Own non-clinical and clinical data?

- study preparation = same as preparation to be marketed
- Posology determined by study results

## Bibliographical clinical and non-clinical data?

- Study preparations equivalent to preparation to be marketed = applicable data?
- Posology corresponds = applicable data?

## No useful clinical data?

- Plausible indication
- Documented safety
- Tradition of use



level of evidence

# Orienting the dossier

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What kind of application type does he chose?

=> based on the level of evidence

=> always the highest possible level

Own non-clinical and clinical data - conform applicable guidelines ?

- FULL APPLICATION

Bibliographical clinical and non-clinical data - conform applicable guidelines ?

- WELL ESTABLISHED USE APPLICATION
  - if criteria are fulfilled (applicable data, time)

No useful clinical data - historical medicinal use documented ?

- TRADITIONAL USE APPLICATION
  - if criteria are fulfilled (TU criteria)



level of evidence

# Preparing the dossier

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## How is the information presented?

Marketing Authorisation Applications or Registration Applications, which should be submitted in either a national or Community procedure consist of :

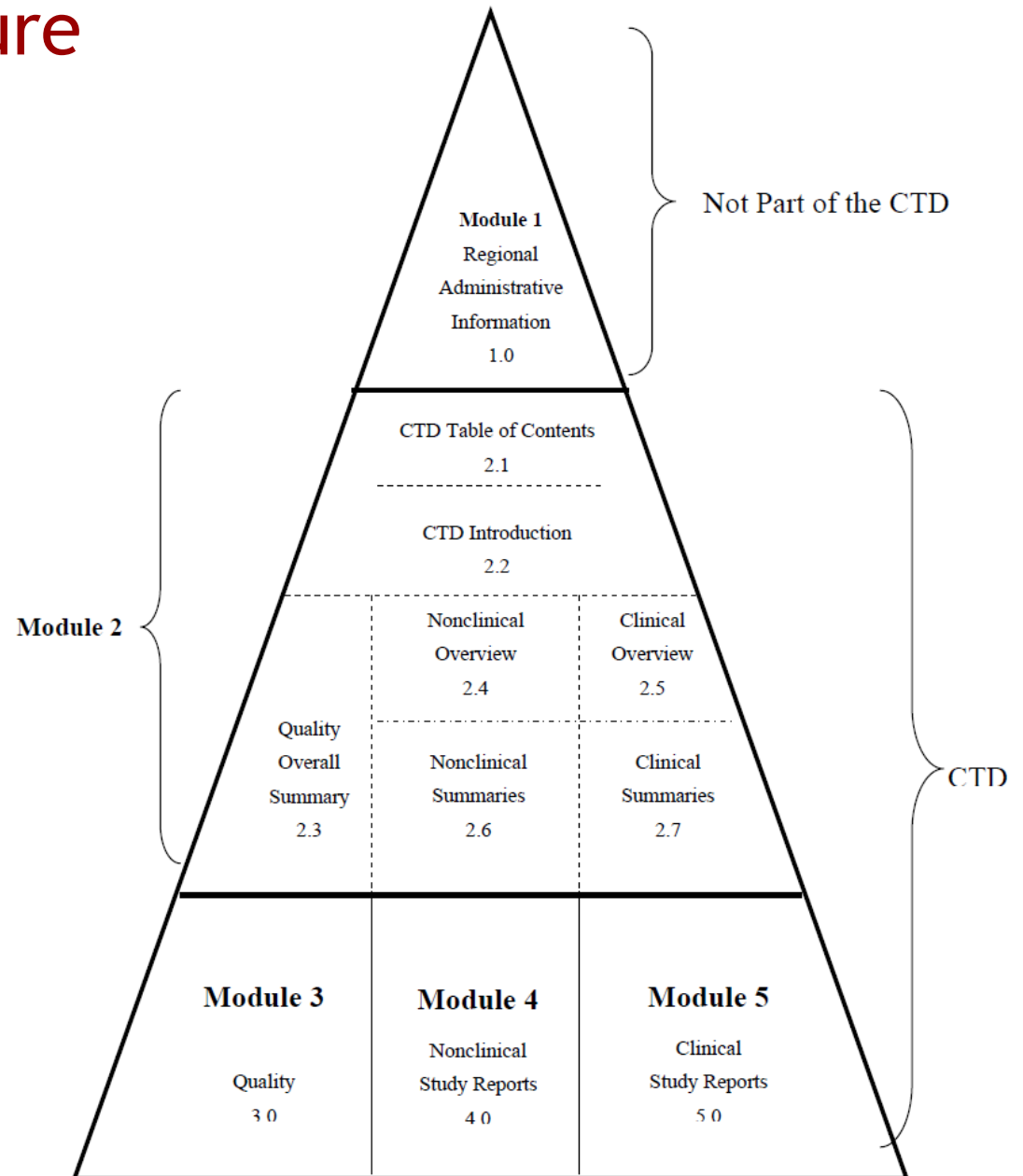
- administrative information -> module 1
- summary of the dossier -> module 2
- the necessary documentation to demonstrate the
  - quality -> module 3
  - safety -> module 4
  - efficacy -> module 5of the product.

All applications have to be made entirely in accordance with the EU-CTD presentation outlined in the NTA, Vol. 2B. (NEES)

=> **ALL** parts and subsections presented

=> contents adapted in function of the dossier requirements

# CTD structure



# Preparing the dossier

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## Traditional herbal medicinal products and CTD:

A guideline on how to present the application for a traditional herbal medicinal product in Common Technical Document format is available on the EMA-website:

<http://www.ema.europa.eu/pdfs/human/hmpc/7104907en.pdf>

## GUIDELINE ON THE USE OF THE CTD FORMAT IN THE PREPARATION OF A REGISTRATION APPLICATION FOR TRADITIONAL HERBAL MEDICINAL PRODUCTS

= all justifications for TU are presented in module 2 with eventual references annexed in module 4 and module 5

(An adapted separate CTD format is a project : **The CONCEPT PAPER ON CTD FOR TRADITIONAL HERBAL MEDICINAL PRODUCTS**)

<http://www.ema.europa.eu/pdfs/human/hmpc/26134405en.pdf>

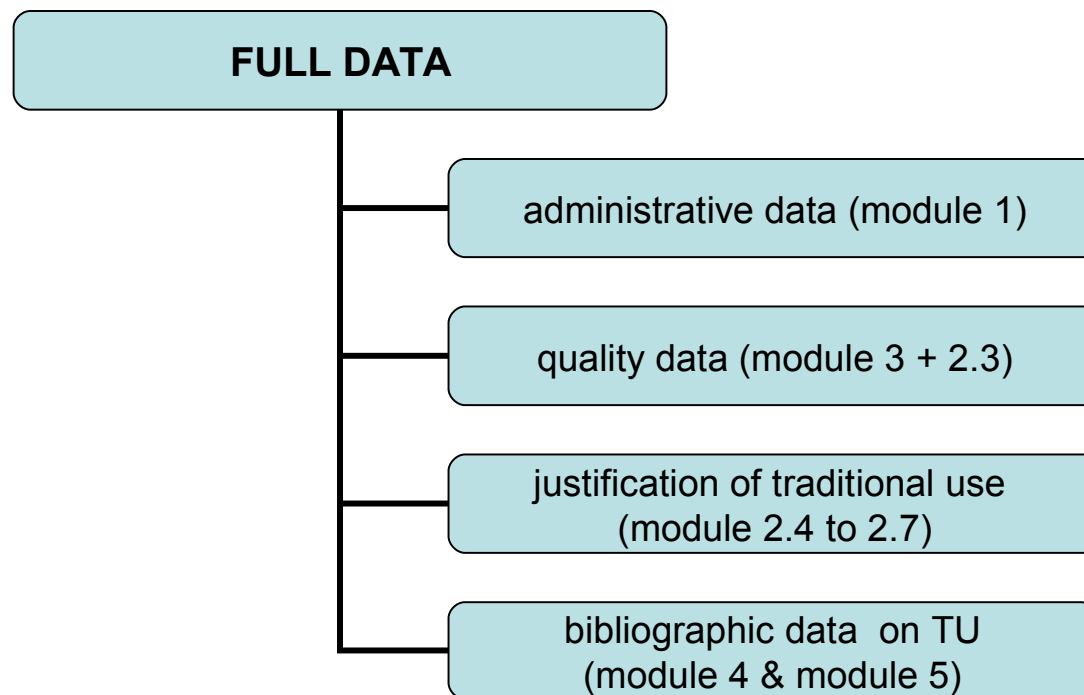
-> Quality part of dossier will always be identical to HMP

# Application for THMP

## APPLICATION BASED ON APPLICANT'S DATA COMPILATION

- no regularization of existing authorization (old legal basis)

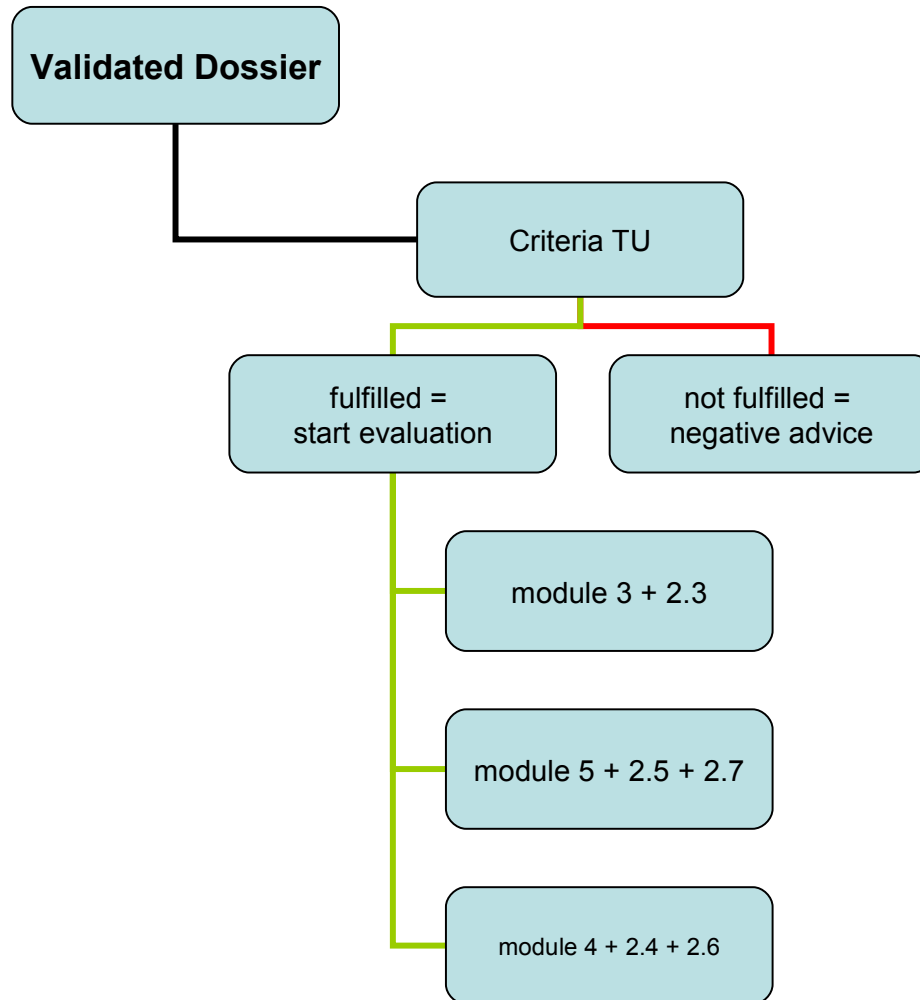
APPLICANT:  
DATA SUBMISSION



# Application for THMP

## APPLICATION BASED ON APPLICANT'S DATA COMPILATION

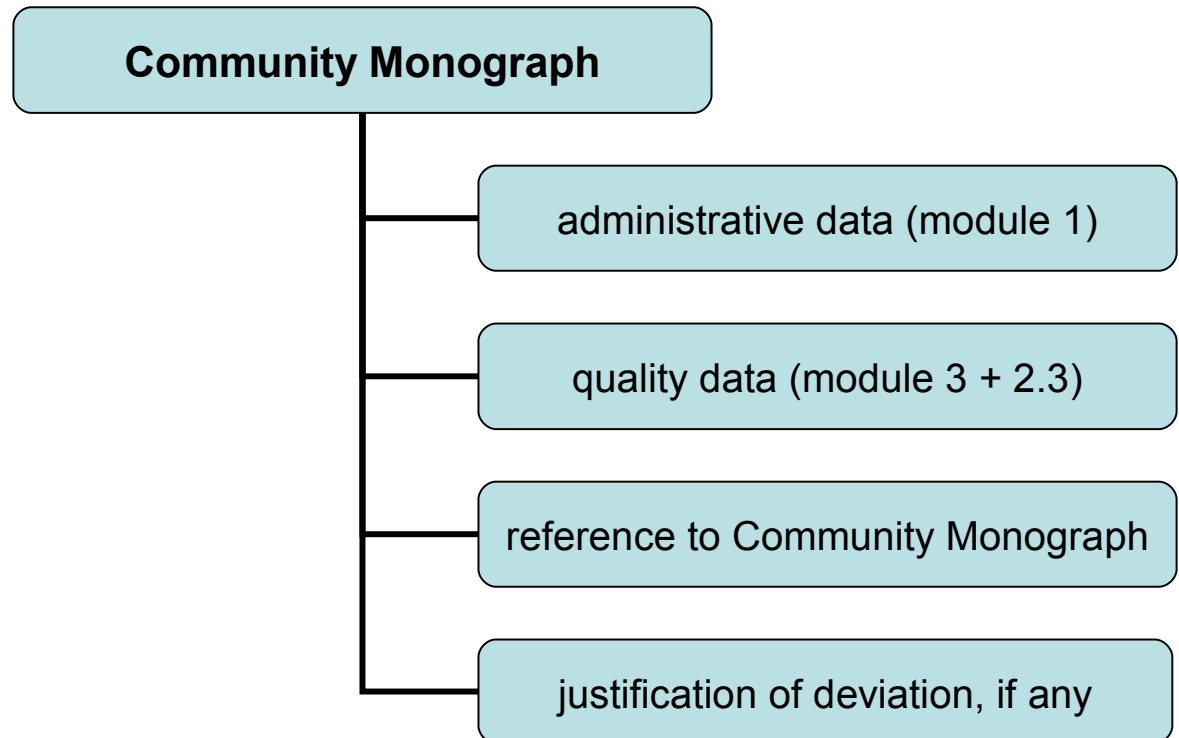
FAMHP:  
EVALUATION



# Application for THMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH

APPLICANT:  
DATA SUBMISSION



# Application for THMP

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## PRACTICAL HANDLING : DEVIATION

APPLICANT:  
DATA SUBMISSION

FAHMP provides services to assist applicants when dealing with possible deviations relating to Community monographs:

### CHECK: ACCEPTABILITY of DEVIATION PRINCIPLE:

- Scientific and/or Technical Advice (AD HOC STA)
- Pre-submission meeting

IF FAMHP accepts the principle, the dossier can be validated as TU-application.

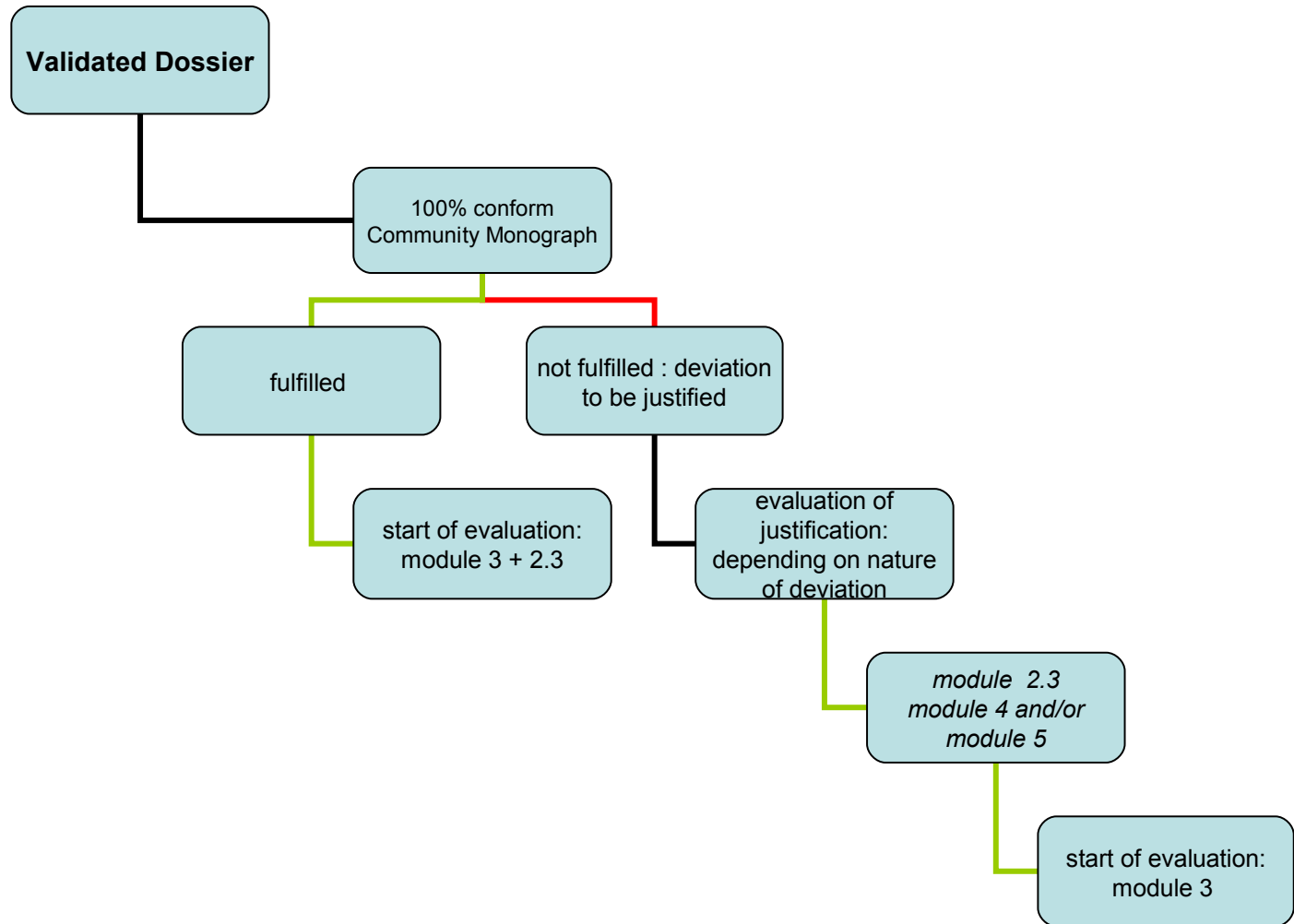
The justification will be evaluated within the context of the submitted dossier.

OTHER: -> involving preliminary evaluation -> Scientific and/or Technical Advice (FULL STA)

# Application for THMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH

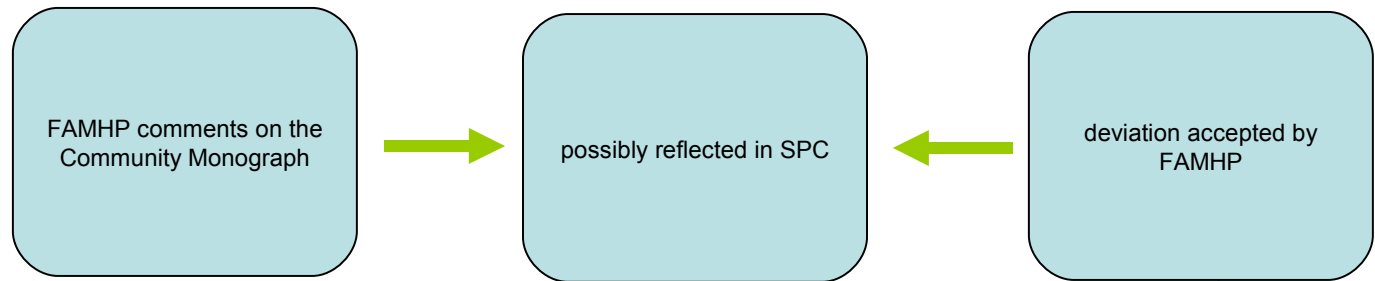
FAMHP:  
EVALUATION



# Application for THMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH

FAMHP:  
ROUND UP



Example: BE allowed different concentration of extraction solvens for *Passiflora*

# Application for THMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH

deviation accepted by  
FAMHP

FAMHP:  
ROUND UP

→ *Passiflora incarnata* L.

Proposed preparations in published monograph:

*Liquid extract (1:8 ; extraction solvent 25% ethanol)*

*Liquid extract (1:8 ; extraction solvent 45% ethanol)*

*Liquid extract (1:1 ; extraction solvent 25% ethanol)*

*Liquid extract (1:1 ; extraction solvent 70% ethanol).*

Preparation proposed by applicant for TU:

*Liquid extract (1:1 ; extraction solvent 60% ethanol).*

Applicants submits Supportive Data:

*Chemical profile + assay*

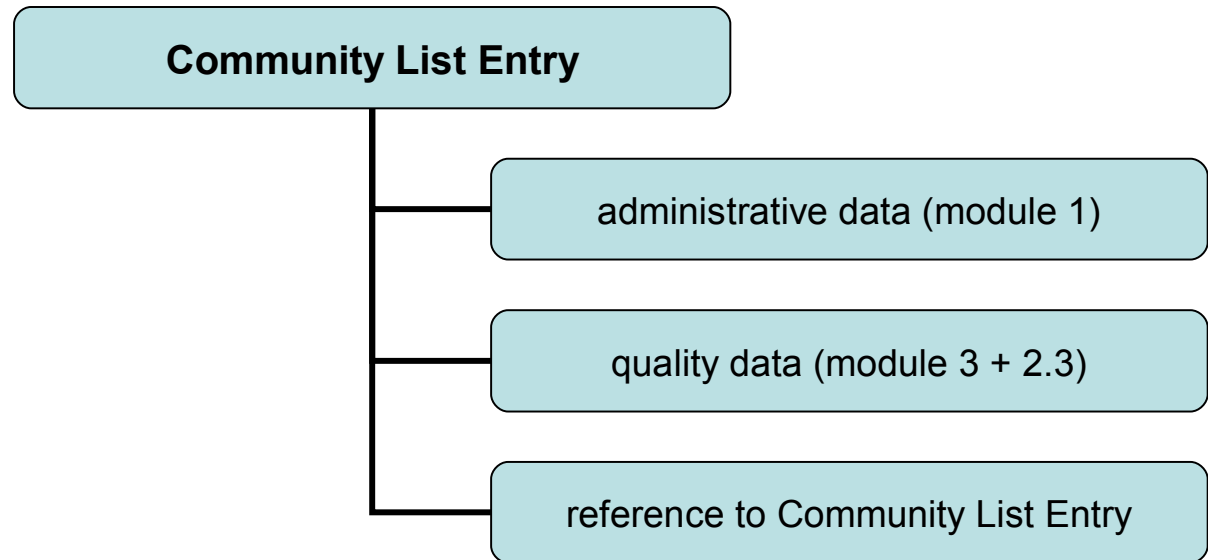
Evaluation of proposed deviation by FAMHP

⇒ BE accepted and allowed the 60% ethanolic extract for the TU application

# Application for THMP

## APPLICATION BASED ON COMMUNITY LIST ENTRY

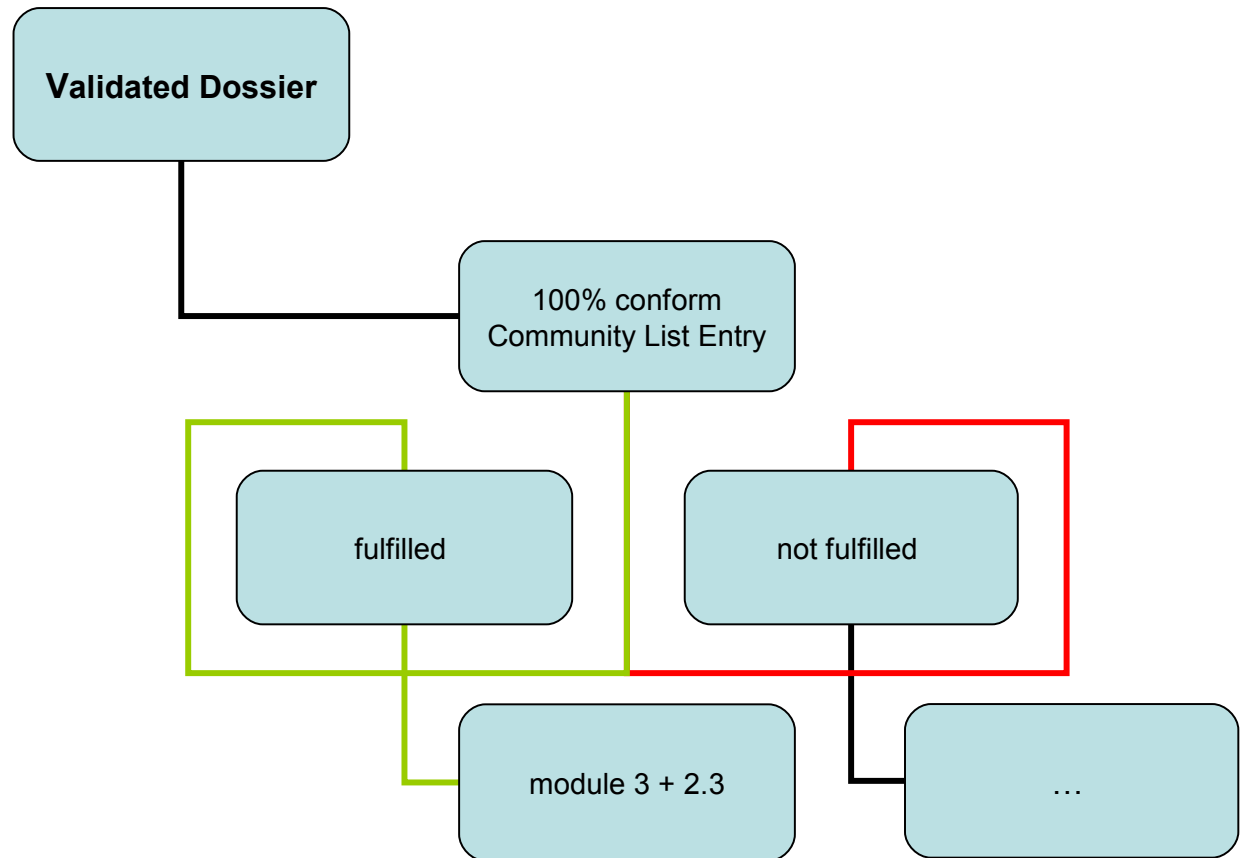
APPLICANT:  
DATA SUBMISSION



# Application for THMP

## APPLICATION BASED ON COMMUNITY LIST ENTRY (1/2)

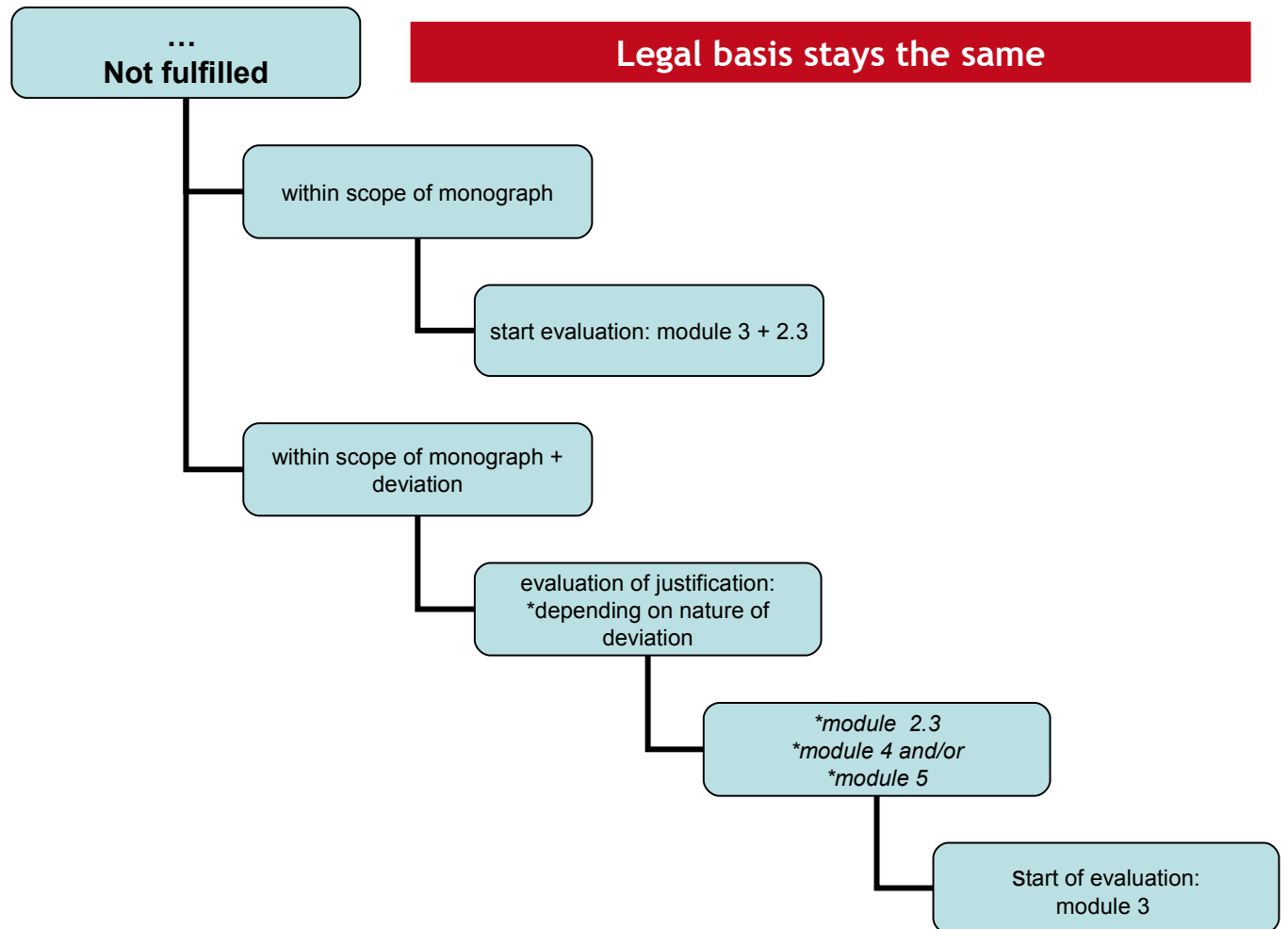
FAMHP:  
EVALUATION



# Application for THMP

## APPLICATION BASED ON COMMUNITY LIST ENTRY (2/2)

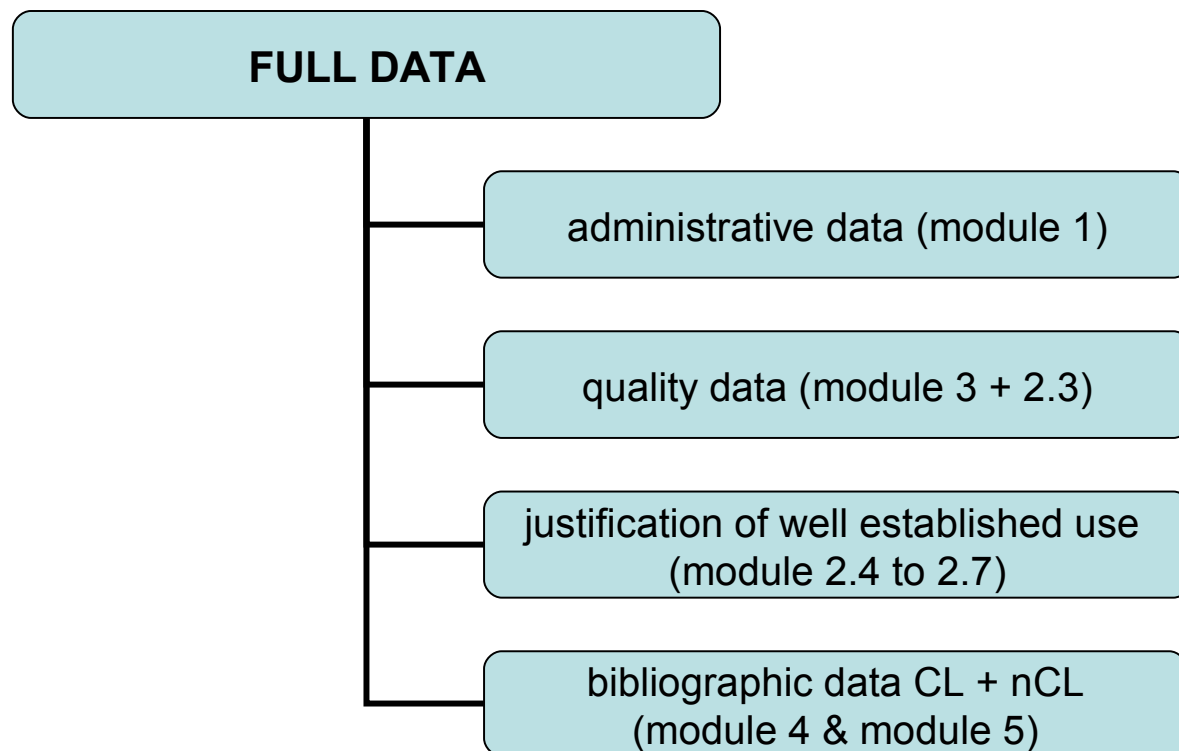
FAMHP:  
EVALUATION



# Application for WEU HMP

## APPLICATION BASED ON APPLICANT'S DATA COMPILATION

APPLICANT:  
DATA SUBMISSION



# Application for WEU HMP

## APPLICATION BASED ON APPLICANT'S DATA COMPILATION

FAMHP:  
EVALUATION

**Validated Dossier**

module 3 + module 2\*

module 4 + module 2\*

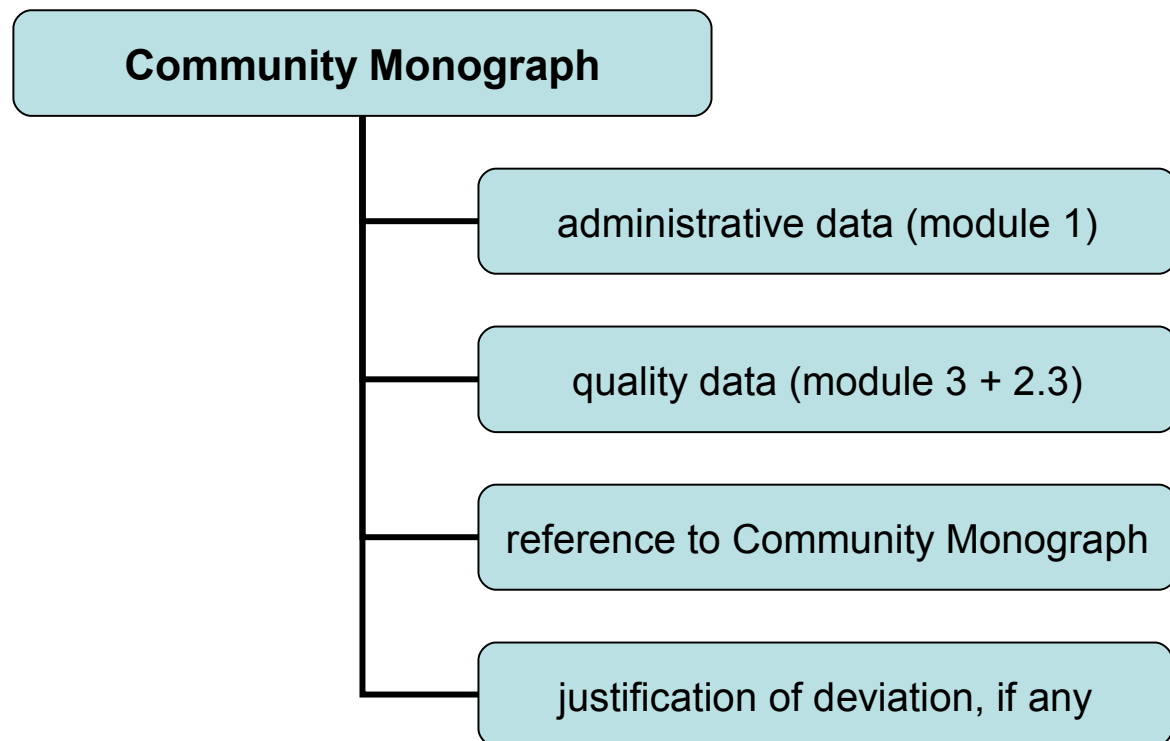
module 5 + module 2\*

\* = applicable sections

# Application for WEU HMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH

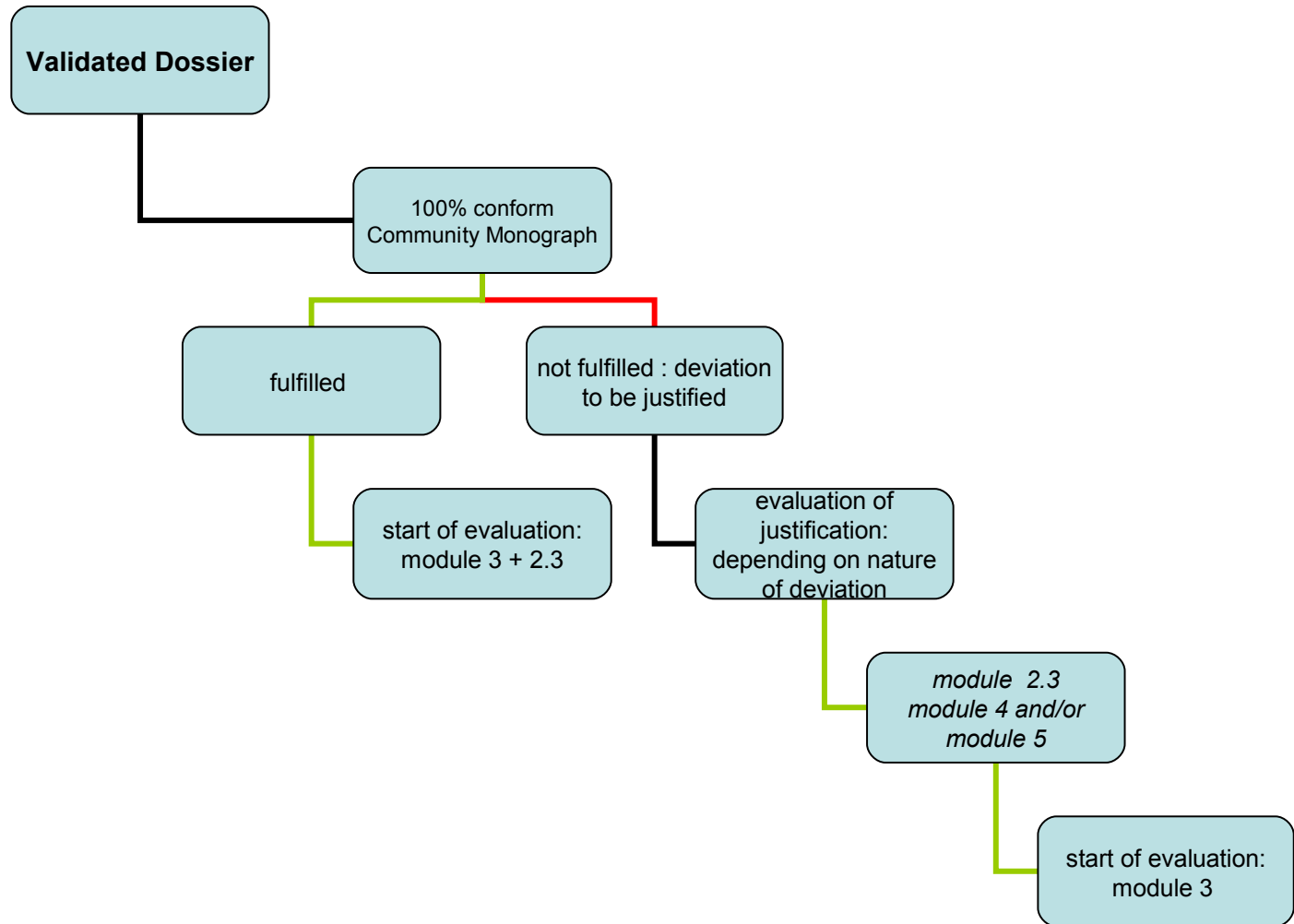
APPLICANT:  
DATA SUBMISSION



# Application for WEU HMP

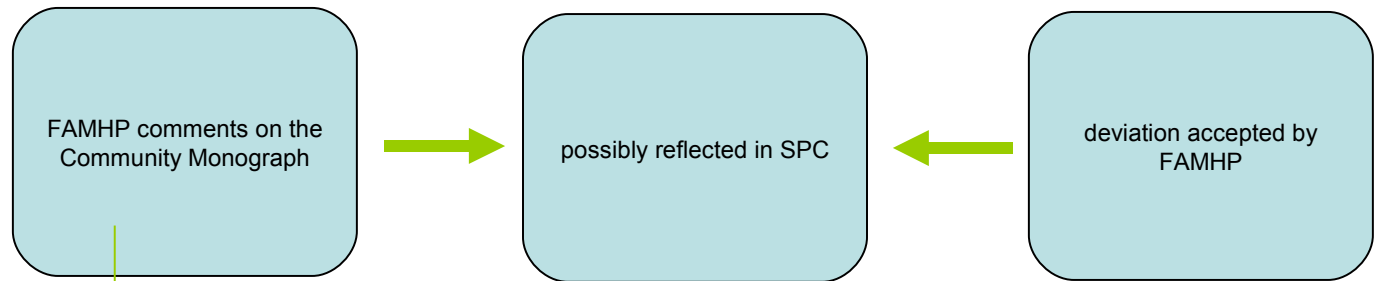
## APPLICATION BASED ON COMMUNITY MONOGRAPH

FAMHP:  
EVALUATION



# Application for WEU HMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH



Example: BE commented on draft monograph for *Hypericum*

FAMHP:  
ROUND UP

# Application for WEU HMP

## APPLICATION BASED ON COMMUNITY MONOGRAPH

FAMHP comments on the  
Community Monograph

FAMHP:  
ROUND UP

→ *Hypericum perforatum* L.

Proposed indication in draft monograph: *Herbal medicinal product for the treatment of mild to moderate depressive episodes (according to ICD-10).*

Indication proposed by BE based on own assessment: *Herbal medicinal product for the short term treatment of reactive depressive symptoms and of mild to moderate depressive symptoms after typical major depressive episodes have been excluded.*

*Taking into account the NFG on clinical investigation of medicinal products in the treatment of depression : <http://www.ema.europa.eu/pdfs/human/ewp/051897en.pdf>*

Comments sent - Monograph approved in unchanged form

⇒ BE follows monograph but deviates for section 4.1:

*Herbal medicinal product for the short term treatment of reactive depressive symptoms and of mild to moderate depressive symptoms after typical major depressive episodes have been excluded*