VolkswagenStiftung

MARTIN-LUTHER-UNIVERSITÄT HALLE-WITTENBERG

MUHAS

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Workshop

# Drug lifecycle control in Subsaharan Africa

## From production to responsible safe disposal and elimination in wastewater treatment plants

(Med4Africa)

# Steps and Considerations in the Galenical Development to Commercial Production of a Pharmaceutical Drug Product

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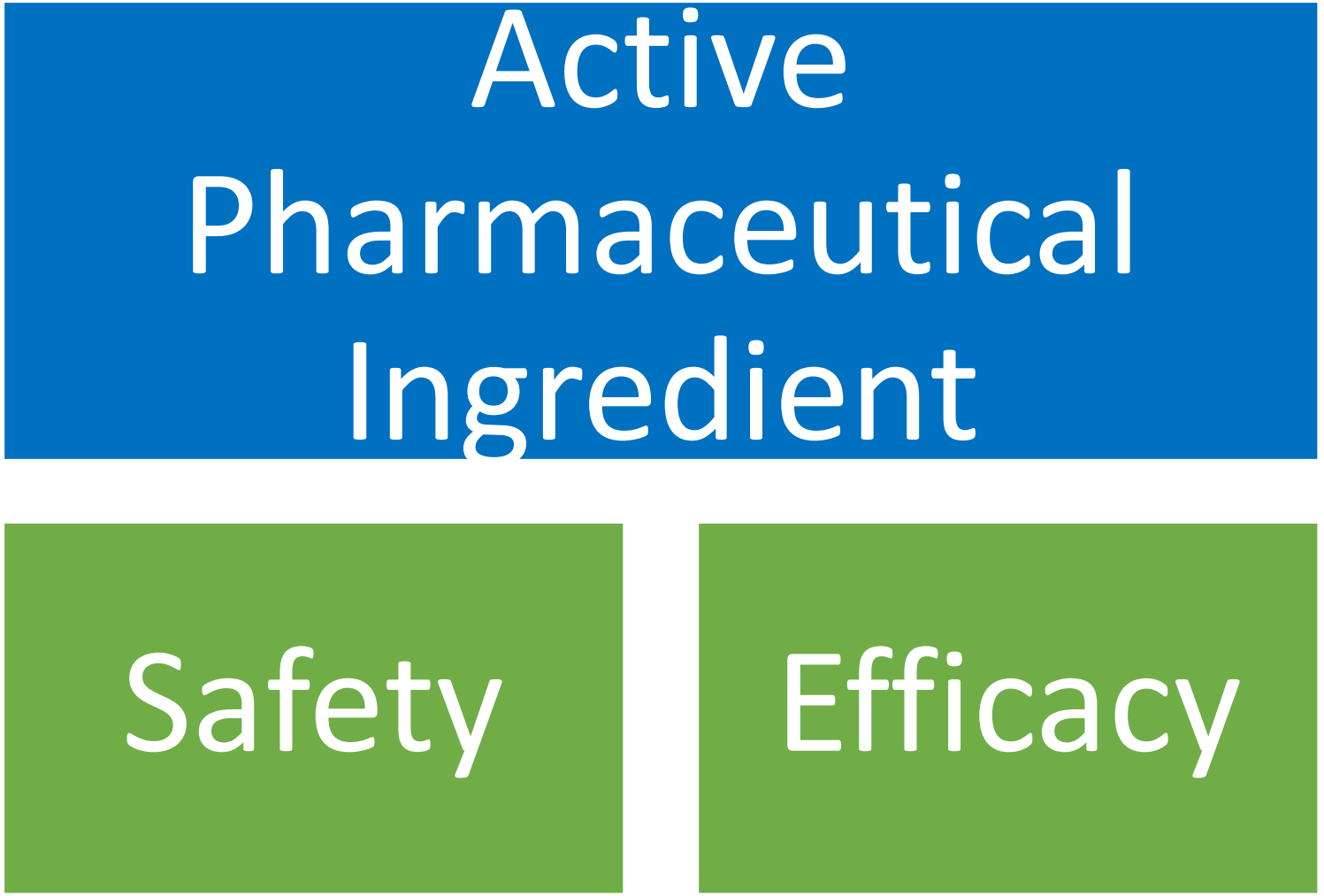
Industrial Pharmacist for 32 years,

Development and manufacturing of pharmaceutical and nutritional delivery forms

Opinions expressed in this presentation are those of the speaker and do not necessarily reflect the views or policies of his employer

# Considerations for the galenical development of a drug product



# API Safety

Therapeutic range

impurities

degradants

formulation design

abuse potential

# API Efficacy

Delivery form

compliance

Patient condition

Patient acceptance

stability

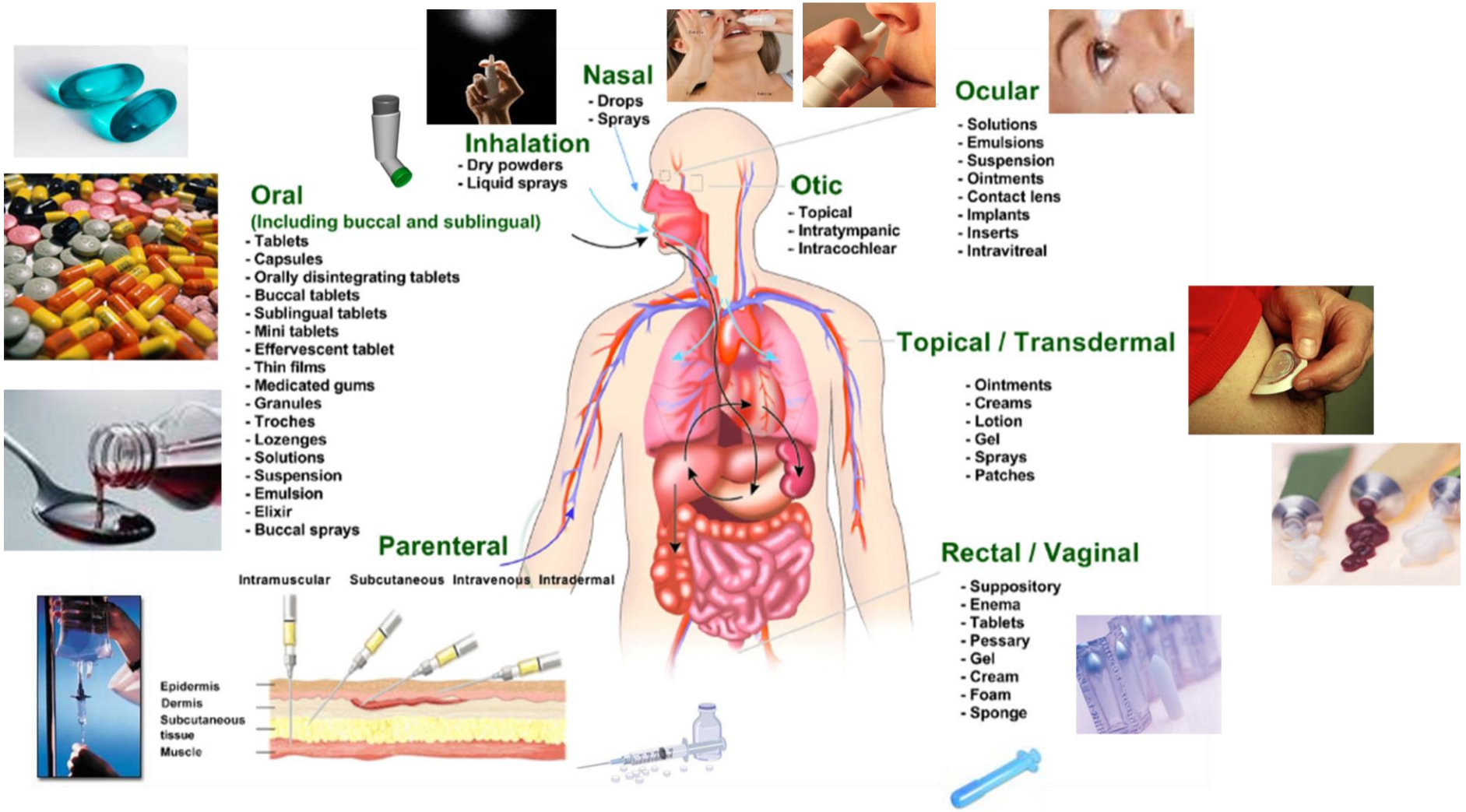
Chemcial / physical

molecul

modification /salts

# Efficacy

Routes of administration



# Delivery Form - Ingredients

- Pharmaceutical active ingredient (API)
- Excipients
  - Inert, formulation supporting function
  - API supporting function

Considerations during selection

Target Profile:

- Dose,
- Delivery form,
- Required properties
- Prescription, OTC, medical device
- Region, countries
  - Stability
  - Regulatory requirements (e,g. Pharmacopeia)
  - Patient compliance factors
- Market expectations, e.g microplastics, allergens, GMO, artifical sweetener & flavors, halal, kosher
- Consumer perception (OTC, Nutritionals)

# Delivery Form - Packaging

- Formulated Delivery form
- Primary packaging
  - Secundary packaging

Consideration during selection

Target Profile:

- API or delivery form sensitivity
  - Temperature
  - Humitdity
  - Light sensitivity
- Cost
- Transportation requirements (ship/air/temperatures)
- Distribution & dispensing system
- Market expectations, e.g Proposition 65, sustainability/recycling
- Consumer perception (OTC, nutritionals)

# Delivery Form - Secundary Packaging

- ICH Q 1 A stabiltity testing including as appropriate secondary packaging

Consideration during selection

Pro:
- additional protection due to additional packaging layer
- light protection of primary packaging not required

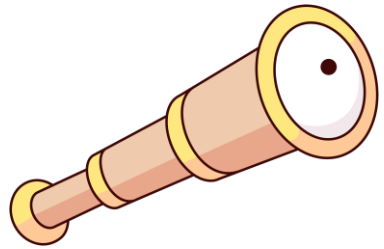
Cons:
- discoloration of carton / paper
- delamination of labels
- artifical odors

- Country requirement
- Dispensing or patient handling

# Development - Preformulation

- Chemical compatibility testing of ingredients with API
- Supporting selection of ingredients, ingredient quality

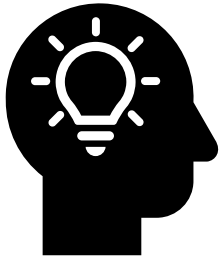
- Small scale galencial formulation trials to explore physical compatibility
- Drafting of a manufacturing process
- Accelerated stability studiess
- Risk assessment
- Cost calculation



Prototypes for internal approval

# Development - Formulation

- Quality Target Product Profile (QTPP)
  - describes the design criteria for the product, and should therefore form the basis for development of the CQAs, CPPs, and control strategy
- Critical Quality Attributes (CQA) - *severity of harm to a*
- *patient (safety and efficacy) resulting from failure to meet that quality attribute*
  - A physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality (ICH Q8
- Critical Process Parameter (CPP)
  - A process parameter whose variability has an impact on a CQA and therefore should be monitored or controlled to ensure the process produces the desired quality. (ICH Q8)
- Critical Material Attribute (CMA)*
  - A physical, chemical, biological or microbiological property or characteristic of an input material that should be within an appropriate limit, range, or distribution to ensure the desired quality of output material.



Planning formulation work

https://pqri.org/wp-content/uploads/2015/10/01-How-to-identify-CQA-CPP-CMA-Final.pdf

# Development - Formulation

- Exploration of ingredients and ratio
- Ingredients documentation
- Exploration of manufacturing processes & variations
- Stability testing in multiple primary packaging
- Testing: e.g light, microbial challenge, packaging, transportation,
- Clinical studies / consumer tests, skin irritation
- Determination of critical material attibutes (CMA)
- Selection of final formulation and manufacturing process
- Definition of design space
- Identification & confirmation of Critical Processing Attributes (CPA),
- Stability studies (ICH)
- Identification of degradants
- Toxicological assessment of formulation and (new) degradants
- Definition of specifications (intermediates and finished product & Critical Quality attributes (CQA)
- Critical material attributes - CMA
- Development report
- Cost calculation

Final formulation

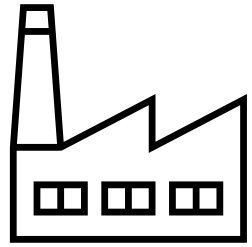
# Development – Scale Up

- Selection of manufacturing site
- Large scale (1/10+ scale)
- 1 -5 experimental batches – process exploration
- Primary packaging trials
- Confirmation / adjustment of design space, and CMA, CPA, CQA
- 1-3 full scale registration batches
- Stabilty testing ICH for registration
- Clinical sample manufacturing
- Cost calculation

- Process Validiation

- Registration documentation

- Control strategy

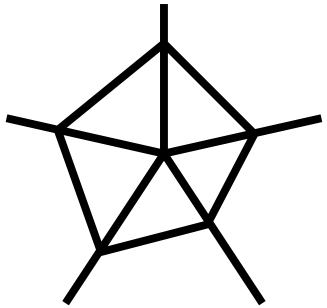


Registration Readiness

# Lifecycle Managment

- Continuous process verification (CPV)
- Product Quality Report (PQR), Annual Product Review (APR)

- Execution control strategy



Quality