Quality by Design in nano-pharmaceutical development: presentation of a software based prediction

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INTRODUCTION

Definition

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management (ICH Q8 (R)).

Characteristics of the QbD concept:

- modern quality management system
- recommended by the Regulatory Authorities (EMA, FDA)
- can be used from basic research until the industrial manufacturing
- systematic
- scientific
- risk-based
- holistic
- proactive approach
- the quality is ensured by design

QbD philosophy: „Quality cannot be tested into products, it should be built in by design"

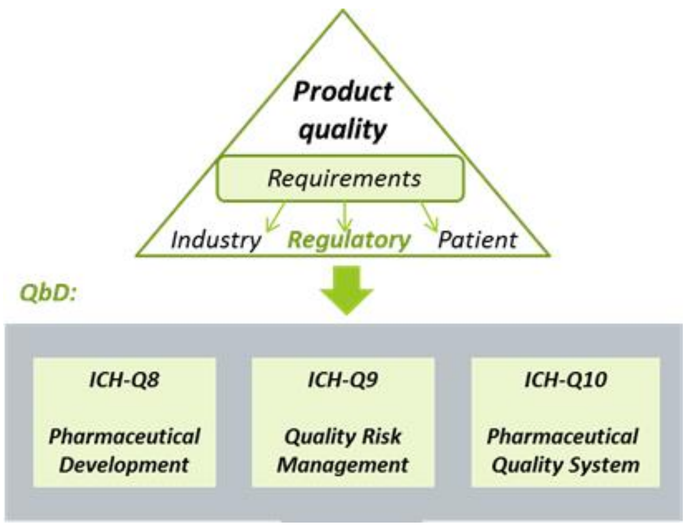


Fig. 1. Pharmaceutical quality requirements and quality guidelines

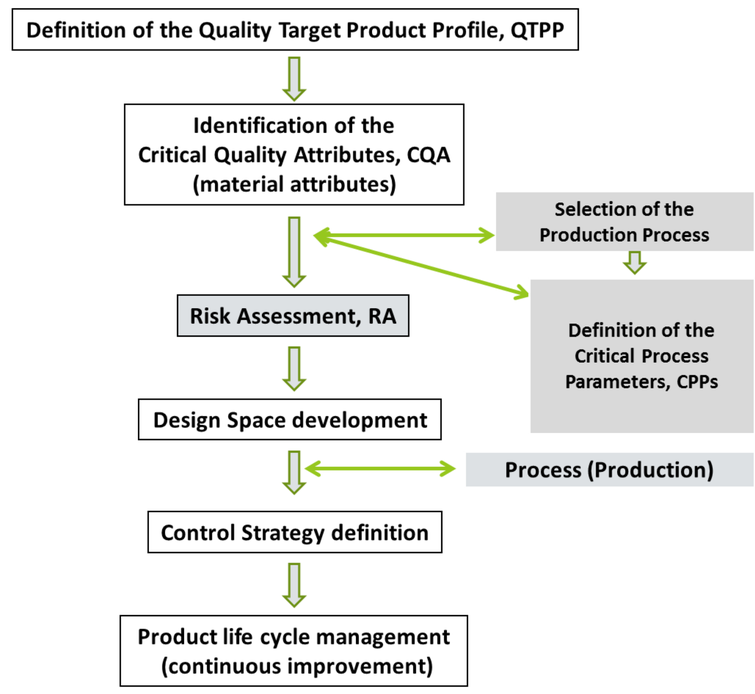


Fig. 2. The steps and the elements of the QbD method

AIMS, METHODS

Aims:

- Applying of the QbD concept in a special early pharmaceutical technological development :
  - Nanosized drug (meloxicam) containing formula
- Present the advantages of a software based theoretical prediction

Methods:

- Special software: „Lean-QbD Software"
- Developer: QbD Works LLC. (Fremont, CA, USA)
- Feature: new possibility of the risk assessment (RA)
- Principle: prior knowledge based (literature and practice)

Benefits and expected results:

- Good RA methodology is priceless
- Theoretical identification and scoring of factors
- Helps in planning the design of experiments
- Helps in focusing of efforts

RESULTS

- **Definition of the QTTP:**
  - Therapeutic indication: pain relief (analgesic)
  - Patient group: adults
  - Administration: alternative route (nasal)
  - Site of activity: systemic effect
  - Dissolution profile: immediate release
  - Active agent profile: nanosized powder
  - Delivery system: gel (for successful application)

- **Selection of materials and production method**
  - Modell active agent: meloxicam
  - Suitable technique: co-grinding

- **Selection of CQAs and CPPs and their interdependence rating results (Fig. 3-4)**

- **Probability rating and its results (Fig. 5-6)**
  - Calculation of impact scores of CQAs and CPPs

- **Relative impact and relative occurrence rating (Fig. 7)**
  - Identification of factors with risk of relatively high occurrence and high impact on the QTPPs

Fig. 3.

CQAs \ CPPs*	Composition	Rotation time	Rotation speed	Grinder's parameters
Excipients	Medium	Low	Low	Low
Size/SA	High	High	High	Medium
Appearance	Low	Low	Low	Low
Dissolution	High	Medium	Medium	Low
Toxicity/Irritation	High	Low	Low	Low
Structure (Cryst./Amorph.)	High	Medium	Medium	Low
Stability	High	Low	Low	Low
Permeability	High	Medium	Medium	Low
Solubility	High	High	High	Low

*CPPs of Co-grinding

Fig. 4.

CQAs \ QTPPs	Therapeutic indication: Analgesia	Target population: Adults	Route of administration: Nasal	Site of activity: Systemic	Dosage design: Nanosized API	Dissolution profile: Immediate release	Production method: Co-grinding
Excipients	Low	Low	Medium	Low	Low	High	Low
Size/SA	Low	Low	High	High	Low	High	Medium
Appearance	Low	Low	Medium	Medium	Medium	Medium	Low
Dissolution	Low	Low	Medium	High	Low	High	Medium
Toxicity/Irritation	Medium	Low	High	Low	Low	Low	Low
Structure (Cryst./Amorph.)	Low	Low	Low	Medium	Low	High	Medium
Stability	Low	Low	Low	Low	Low	Low	Medium
Permeability	Low	Low	High	High	Low	High	Medium
Solubility	Low	Low	Medium	High	Low	High	High

Fig. 5.

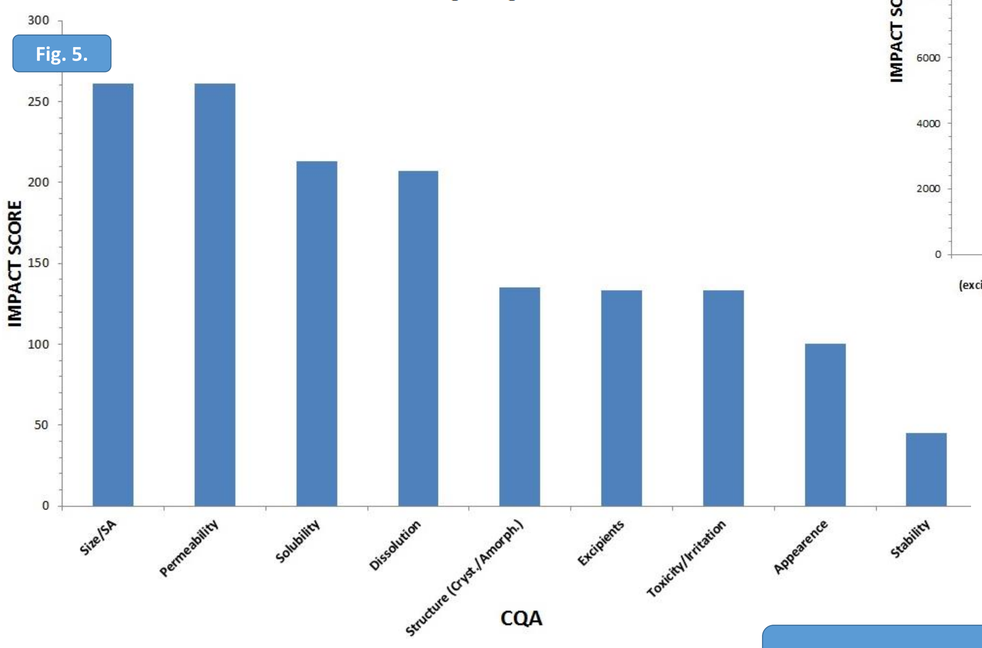


Fig. 6.

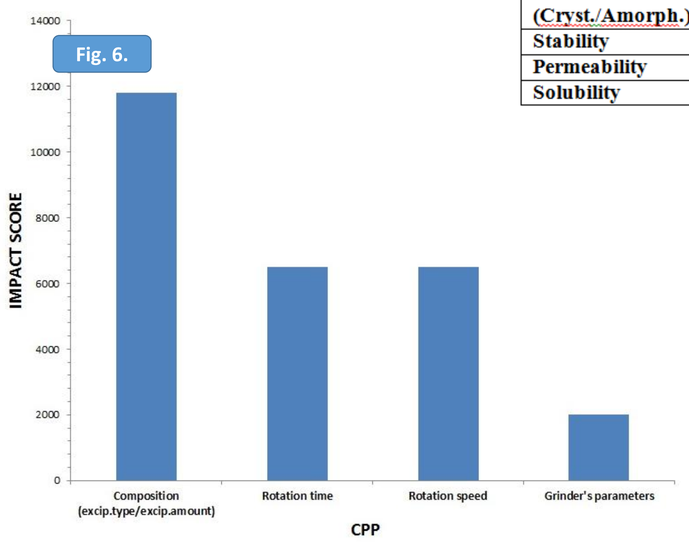
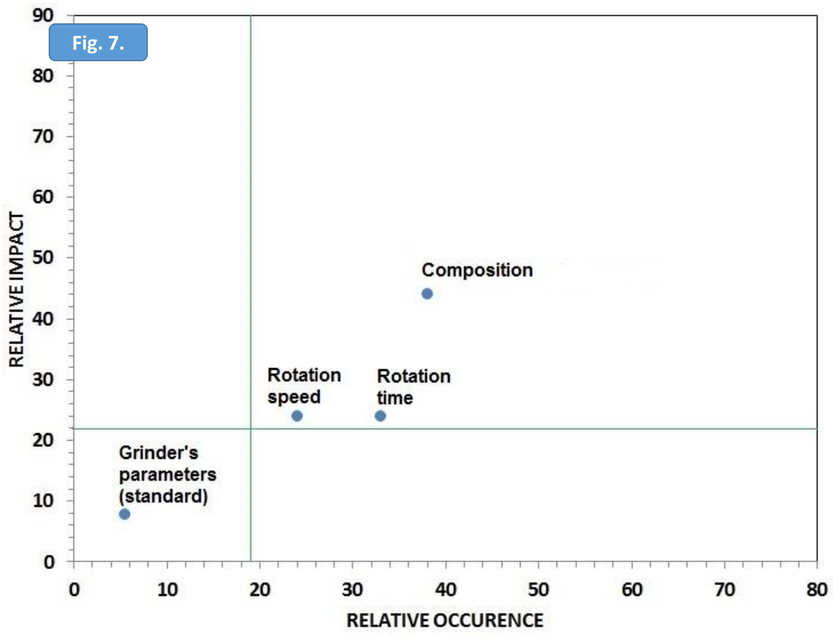


Fig. 7.



SUMMARY, CONCLUSION

- QbD is well applicable also is special (nano) early developments
- The QbD based academic research promotes the nearing of science and the industry.
- A software based RA can predict theoretically the factors (the CQAs and the CPPs) with highest influence on the product quality.
- This QbD based prediction results in shorter development time, lower cost, spare in human resource and more effective target-orientation in practical development.
- These are important in case of developments which are expensive, time-consuming and complex like nano-technological experiments.

- **Details:**

Please read and cite our latest article:
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