Quality by Design approach in pharmaceutical and cosmetic research and industry: strategic thinking for international competitiveness

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Introduction

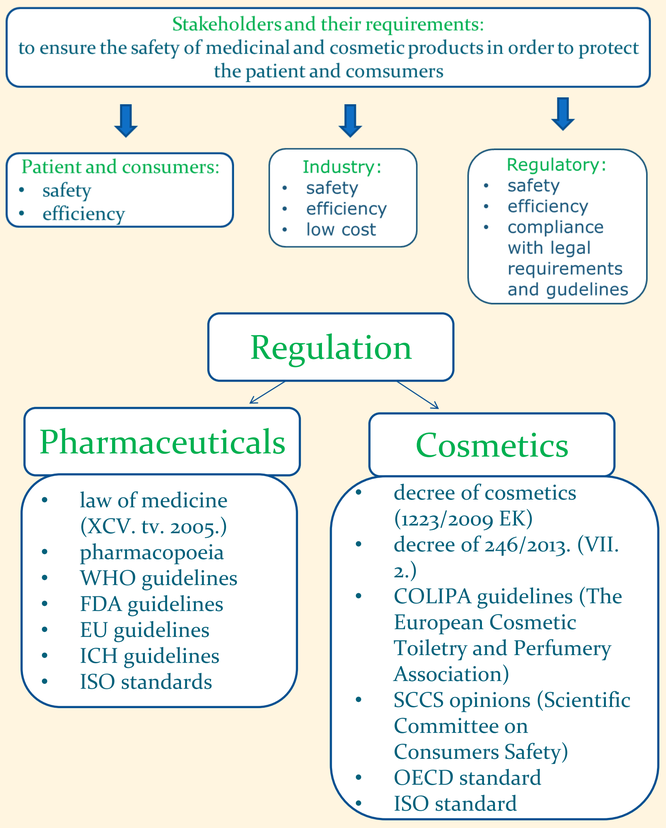
The consumers requirements for products in the fields of both cosmetic and pharmaceutical industry change continuously. In order to meet the changing requirements and keep the competitiveness, the manufacturing companies have to continuously improve the quality.

However, the QbD concept is requested mainly from manufacturers, also research organizations within pharmaceutical and cosmetic field can use this methodology in their product development to achieve Shiba's highest level of quality and ensuring their competitiveness within this market.

Aim of this study

- to highlight the most important guidelines and practices of quality in the pharmaceutical and cosmetic industry
- quality by design (QbD) approach adaptation for product development of pharmaceutical and cosmetic product within a case study of a dermal product development based on QbD approach is presented

To produce appropiate quality product, we had to know the stakeholders of the product and their requirements.



ICH (International conference harmonization) guidelines

Quality by Design (QbD) in general meaning is a systematic process to build quality into a product from the inception to final output. This term is also defined by the FDA and is world-widely published in ICH Q 8 Guideline as 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.

Method

A case study of a dermal product development based on QbD approach is presented. The general PDCA cycle combined with the QbD steps was used in the pilot study (Figure 1).

Reference

A.Kovács, I. Erős, I.Csóka, Optimization and development of stable w/o/w cosmetic multilpe emulsions by means of the Quality by Design, International Journal of Cosmetic Science, 1-11 (2015), doi: 10. 1111/ics.12248

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Results

PDCA cycle combined with the QbD concept

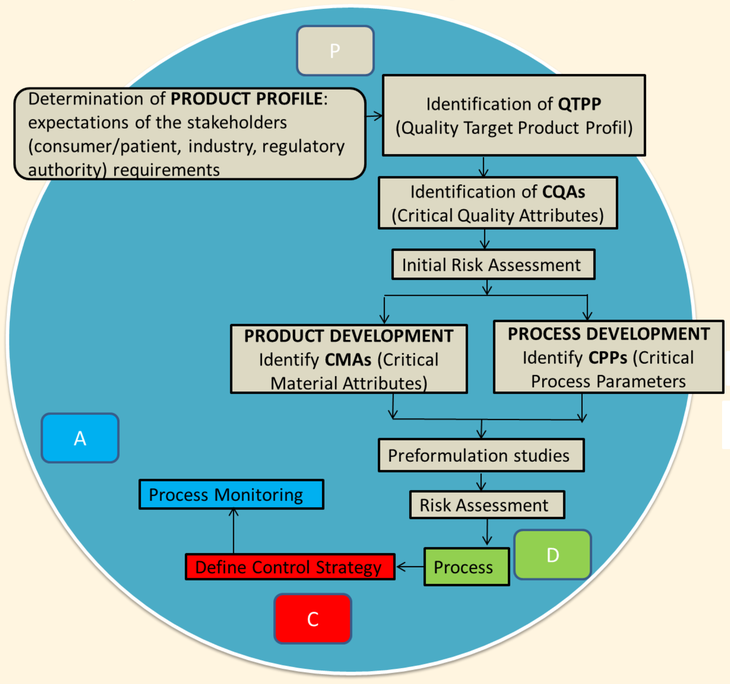

Figure 1: General PDCA cycle combined with the QbD steps

Case study of a dermal product development based on QbD approach

The process of quality target product profile (QTPP) and critical quality attributes (CQAs) determination, selection of the critical material (CMAs) and process parameters (CPPs) based on the requirements and expectations of the stakeholders are presented. These data we got were found to be very important for **risk assessment** and to ensure that the product development provides a stable dermal product of excellent quality.

Table I: defining QTTP (Quality Target Product Profile) and CQAs

QTTP parameters	Target	Justification	Is this CQA?
Dosage form	o/w emulsion	Pharmaceutical and cosmetic requirement	
Dosage design	oil in water emulsion cream with active agent/API in the cream base	Pharmaceutical and cosmetic requirement	
Route of administration	topical	Pharmaceutical and cosmetic requirement	
Homogeneity and tube uniformity	bottom, middle and top of three containers	Needed for proper effect	YES
Container closure system	bottles	Needed for safety and commercial requirements	
Stability: physico-chemical, microbiol.	at least 12 months shelf-life at room temperature	Needed for commercialization: degradation product, packaging	YES
Dissolution	match reference listed drug/active agent	Required to demonstrate ICH Q3, or other guidance/standand	YES
Physical attributes (colour, odour, appearance)	acceptable to patients	Physical attributes were not considered as critical	
Droplet size	from 100nm to 100µm	it was considered as critical for stability	YES
Droplet structure	simple	it was considered as critical for stability	
pH	4-8	it was considered as critical for stability	YES
Viscosity	tested	Required to demonstrate Q3	
Particle size of API or active agent	>100nm	it was considered as critical	YES
Microbial limits	Meet USP <61> decree of cosmetics	Needed for safety	YES
Residual solvents	Meet USP <467> or decree of cosmetics	Needed for safety	YES
Mean dissolution time	low	it was no considered as critical for stability	
Drug release	high	it was no considered as critical for stability	

Initial Risk Assessment for Product Development

The following initial risk assessment screens critical factors.

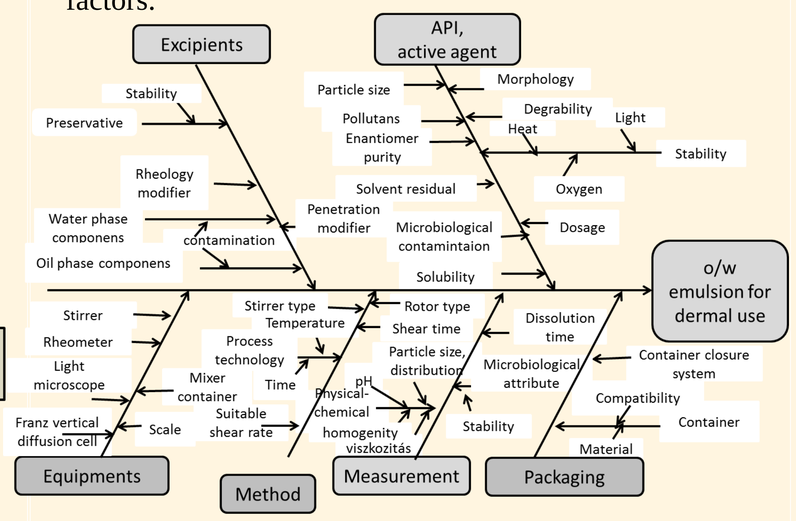

Figure 2 Ishikawa Fish-bone diagram defining the causality relationships between the compositions and process parameters for emulsions

Table II.:Initial Risk Assessment for process parameters

Process parameter	Risk factors	Is it has effect for CQAs?
Process technology	physical stability	YES
Stirrer type	particle size, morphology	NO
Shear rate	particle size, morphology homogenity, viscosity	YES
Shear time	homogenity, viscosity	YES
Rotor type	particle size, morphology	NO

Table III: The risk estimation matrix (Lean-QbD Software): Low=low risk parameter; Medium=medium risk parameter; High= high risk parameter

CQA - CPP/CMA

Process / CPP/CMA / CQA		Process technolog	Stirrer type	Rotor type	Shear rate	Shear time
		26%	16%	16%	28%	15%
Homogenity	13%	Medium	Low	Medium	High	Medium
Stability	19%	High	Medium	Low	Medium	Low
Droplet size	13%	High	Low	Medium	High	Low
pH	13%	Low	Low	Low	Low	Low
API/active agent	22%	Medium	Low	Low	Medium	Low
Dissolution	22%	Low	Low	Low	Medium	Low

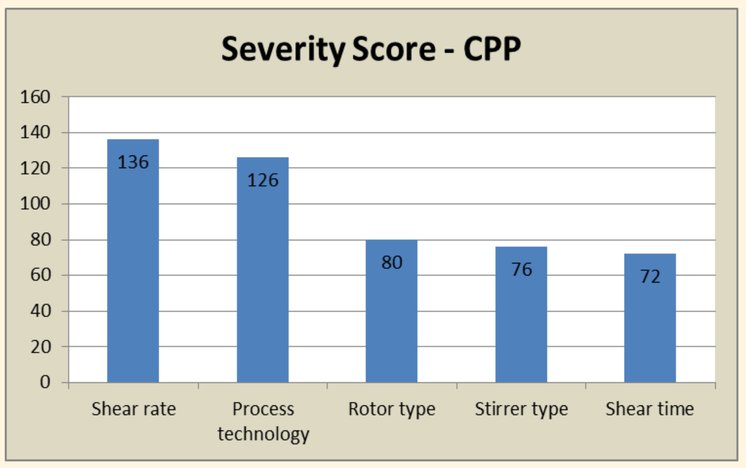

Figure 3:Pareto chart for screening critical process parameters can ensure stable dermal product.

The Pareto chart shows the severity scores and the parameters that had severity scores higher than 100 were considered necessary examination.

Based on the results of risk assessment two factors, namely shear rate and process technology, were found to be highly critical factors for CQAs.

Summary

The QbD based development in the research phase, focusing on more careful planning in determining quality target product profile (QTPP), critical material attributes (CMAs), critical process parameters (CPPs) and critical quality attributes (CQAs) - important for the regulatory body and industrial partners and also including the patient/customer preferences - showed to be a time and cost saving procedure.

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