IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

Management of Device Changes Through the Product Lifecycle

Carla Vozone on behalf of IPAC-RS

An Association Focused on Scientifically Driven Advancements in Development and Regulation

- Companies that develop, manufacture or market orally inhaled and nasal drug products (OINDP)
  - OINDPs are drug-device combination products with CDER as primary review division
- Mission: Advance scientifically driven approaches to enhancing product quality of inhaled and intranasal drug products for the benefit of patients.

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Management of Device Changes Through the Product Lifecycle

Situation

- There is significant variability as to how companies manage device design changes. This is supported by a survey conducted by IPAC-RS.

Target

- Regulators, member companies and therefore patients would benefit significantly if industry adopted a common framework for the management of device changes.

Proposal

- It is proposed to adopt a common framework for the management of device changes. This framework is based upon a risk based approach to product development as defined in ICH Q8, Q9 and Q10.

Why Guidance? Defining a process for infinite design changes for an infinite number of potential devices is not practicable

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Situation – Validating the Problem Statement

Method

A survey was conducted of all members companies

The survey identified 15 scenarios sub-divided into 3 categories

- Design, Materials and Manufacturing Processes

For each scenario respondents were required to confirm;

- What, if any, in-vitro testing would they conduct to support the change
  - Chemical Analysis & Mechanical Robustness
- What, if any, in-vivo testing would they conduct
  - Patient Handling Studies, Pharmacokinetic, Pharmacodynamic
- Why were they conducting the testing?
  - to satisfy an internal design development change control management process
  - to satisfy a regulatory requirement
  - both
- How they would notify the regulatory authorities of the change?

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Situation – Validating the Problem Statement

Scenario 3 (of 15)	
Focus area	Design Change
Stage	Clinical Phase 2b (dose – ranging) completed and considering a start on clinical Phase 3
Description	A novel beta-2-agonist inhaled drug product (DPI) is under development. As a result of feedback from intended users and opinions from several focus groups, it is proposed to modify the mouthpiece to be longer and slightly wider.

Total Number of Respondents 105

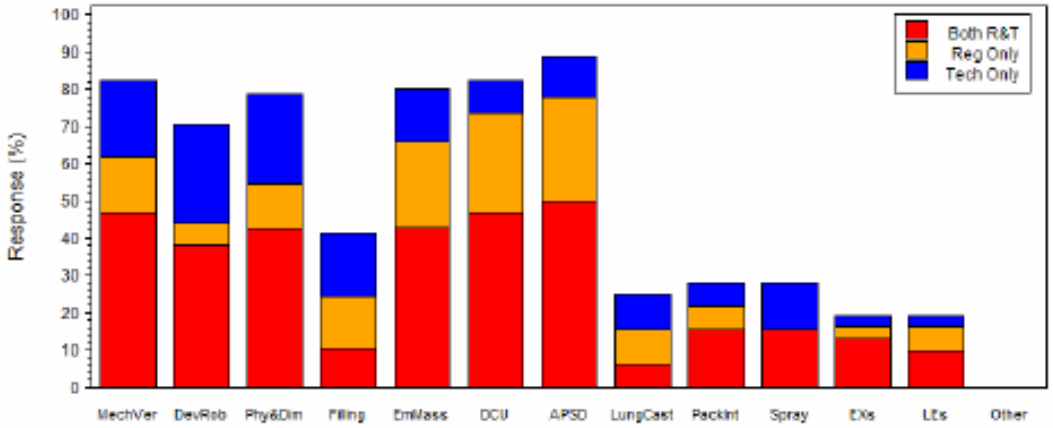
- Testing for internal change management
- Testing to satisfy regulatory requirement
- Both

Context	N
NDA or EQ	30
ANDA or EQ	7
No Answer	68

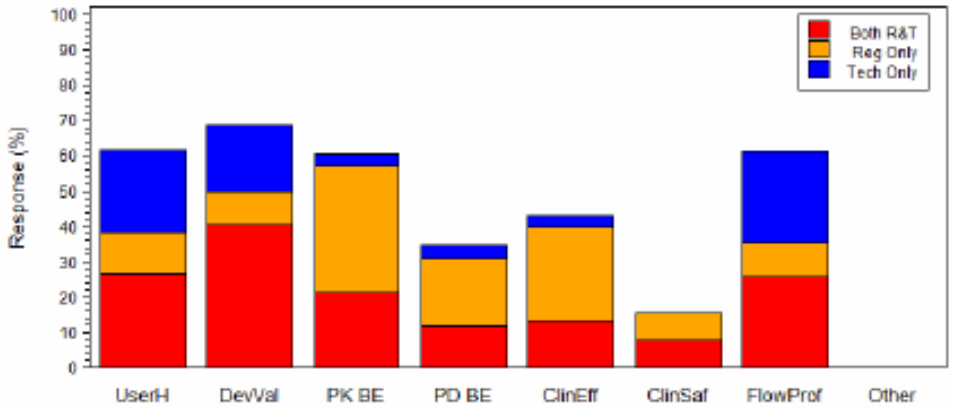
Submission	N
Update IND/CTA	24
PAS or EQ	4
Suppl. CBE30	2
Suppl. CBE	1
Ann. Rep or EQ	1
No Submission	1
No Answer	72

Months	25/60	30/60	40/75
No Test /0	12	12	12
3	3	3	5
6	3	2	12
9	0	1	0
12	4	6	1
18	0	0	0
24	9	3	0
No Answer	74	78	75

Scenario 3: Non-clinical testing



Scenario 3: Clinical testing



Situation – What Did the Survey Tell Us?

- A lack of consistency in how members companies both manage the change process and how they notify regulatory authorities.

- Risk Management, as defined by ICH, does not appear to be informing decision making.

- Supports the development of guidance utilising a risk based management approach to evaluate and manage device changes for OINDP could be of significant value to all stakeholders

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Target – Defining the Solution

Scope

- All “Combination Products ” post start of Pivotal Clinical Studies, pre and post market authorisation, are within the scope of this proposal.

- The proposed guidance relates to product lifecycle management of device changes.

- The process is applicable to the development of a generic or an innovator product. It describes the work that should be conducted as a given Device A evolves through the product lifecycle.

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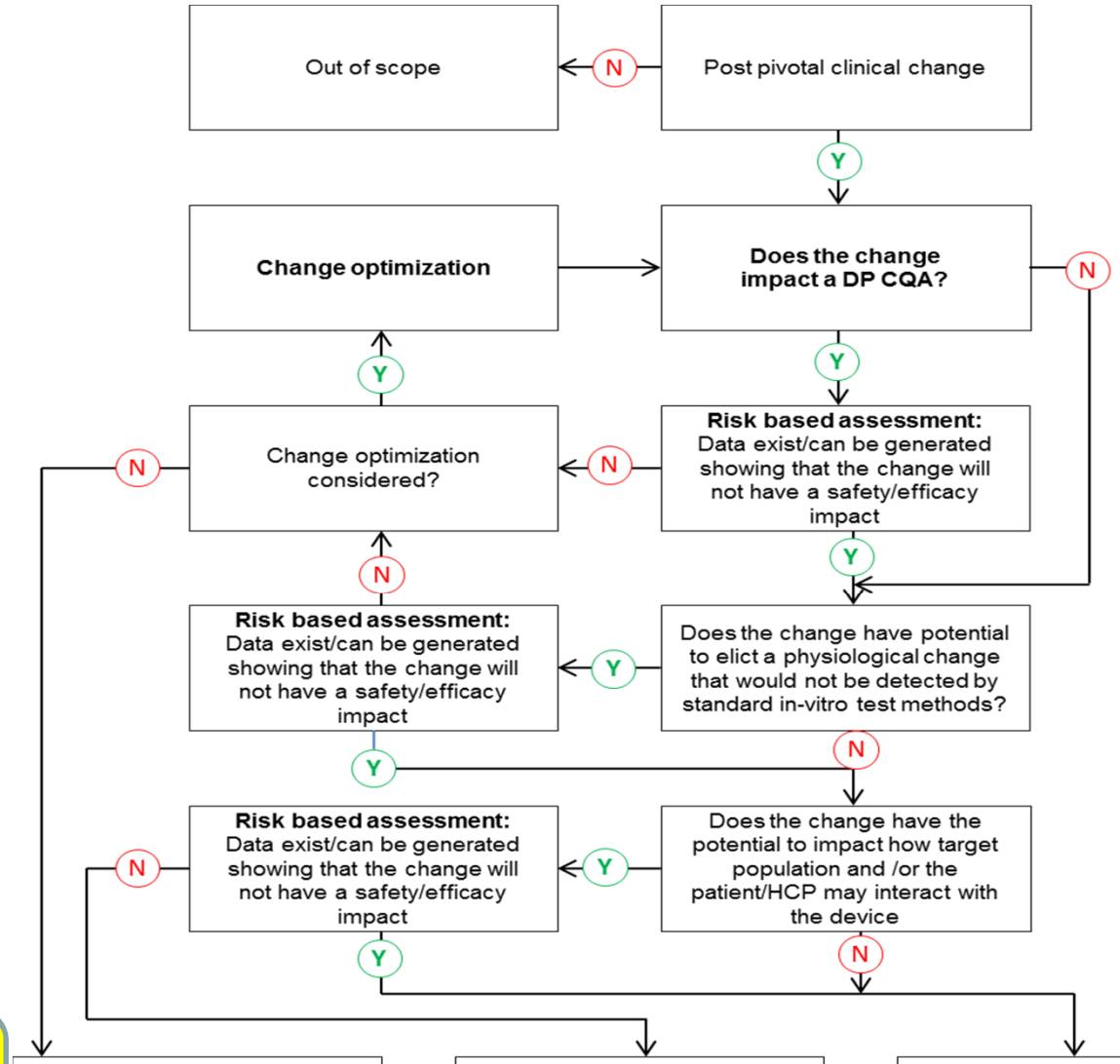
Proposal – A Risk Based Approach to Management of Device Changes Through the Product Lifecycle



Sponsoring company to determine the type of clinical bridging study to be conducted

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Conclusion

- This survey shows that industry follows different criteria to make assessment of changes and indicates lack of consistency in approaches that may affect the development of devices for generics as well.

- The study supports the need for device guidance in generics development.

- Based on this, IPAC-RS recommends that FDA consider assessing:
  - Differences in how change management is currently approached (demonstrated by this survey)
  - The impact of adopting a common framework for risk-based device change management through the product lifecycle

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