

# IQ Risk Based Predictive Stability Working Group

Regulatory Sub-Team

# The Team

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- Debra Webb
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- Helen Williams
  - AstraZeneca
- Yan Wu
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# Regulatory Sub-Team Goals

## **Current Focus**

Conduct industry survey to get a sense of to what extent Risk Based Predictive Stability (RBPS) are being utilized in regulatory filings along with the regulatory experience.

Publish the results

## **Additional Short Term Goal**

Publish regulatory experience around multiple cases studies (potential overlap with other sub-teams). In conjunction with webinar/workshop.

## **Long Term Goal**

Harmonize the level of detail and publish a formatted template that could be used for regulatory filings.

Lobby ICH to update Q1A of publish a Q1A Q&A document regarding RBPS.

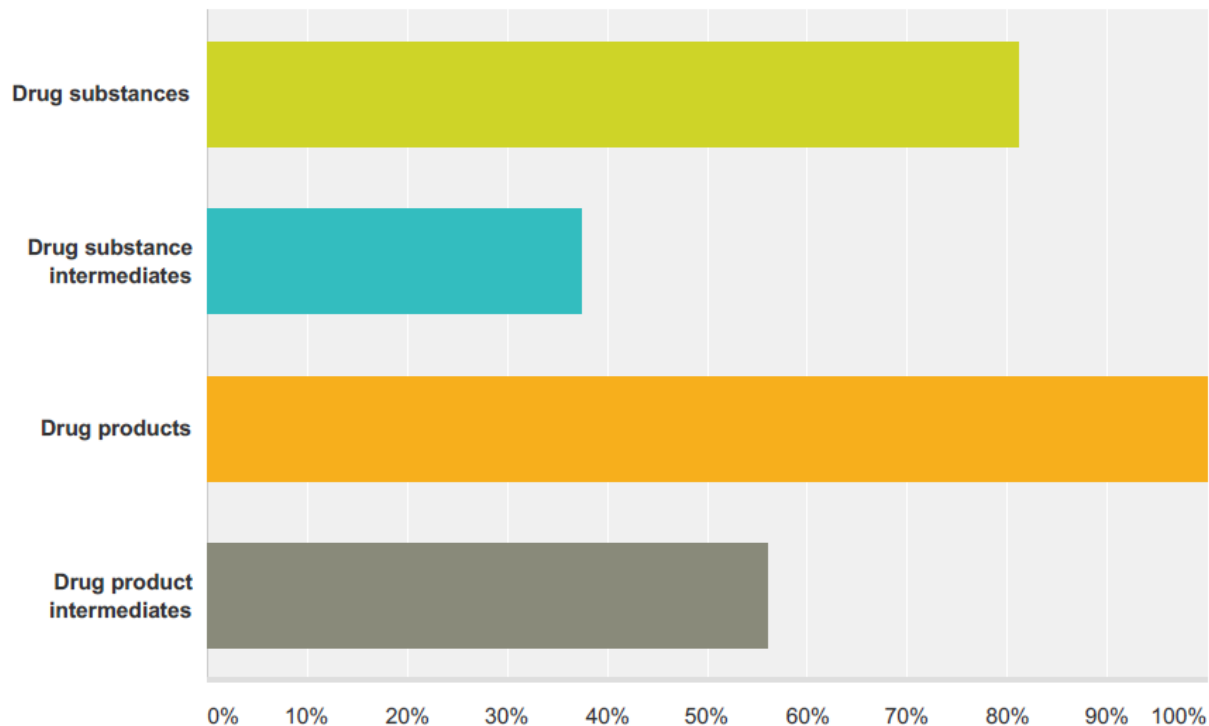
Leverage findings with regional policy groups via company regulatory policy groups.

# Survey Details

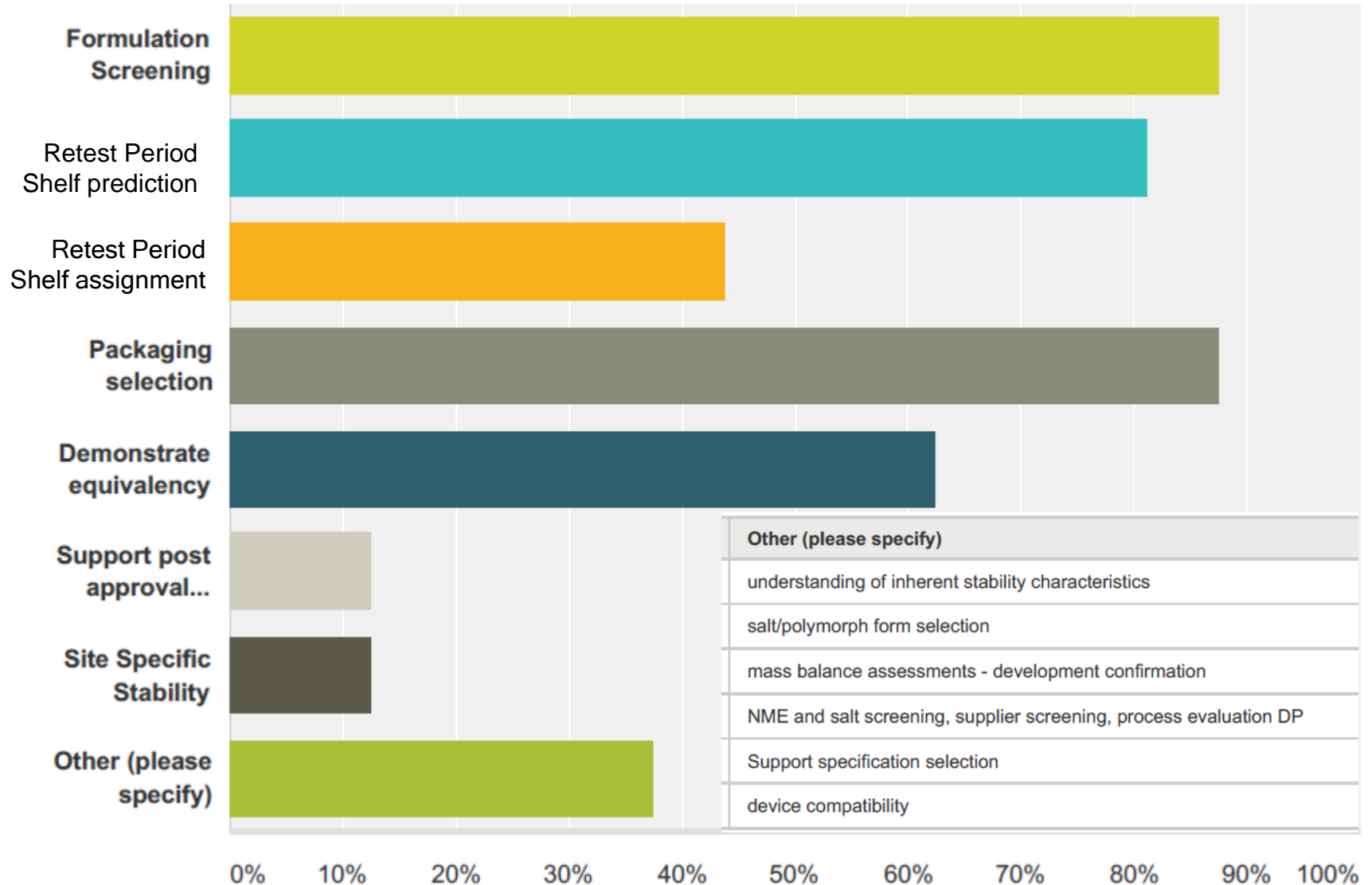
- 56 Questions
- Survey Distributed to IQ Analytical Leadership Group (33 Companies)
- 19 companies responded
  - 58% Response Rate
    - 100% NME's, 11% Generics

# Risk Based Predictive Stability (RBPS)

- 84% (16/19) Have used risk based predictive stability designs
  - 94% Small Molecules
  - 19% Large Molecules
- Types of materials Studied



# RBPS used in a variety of applications

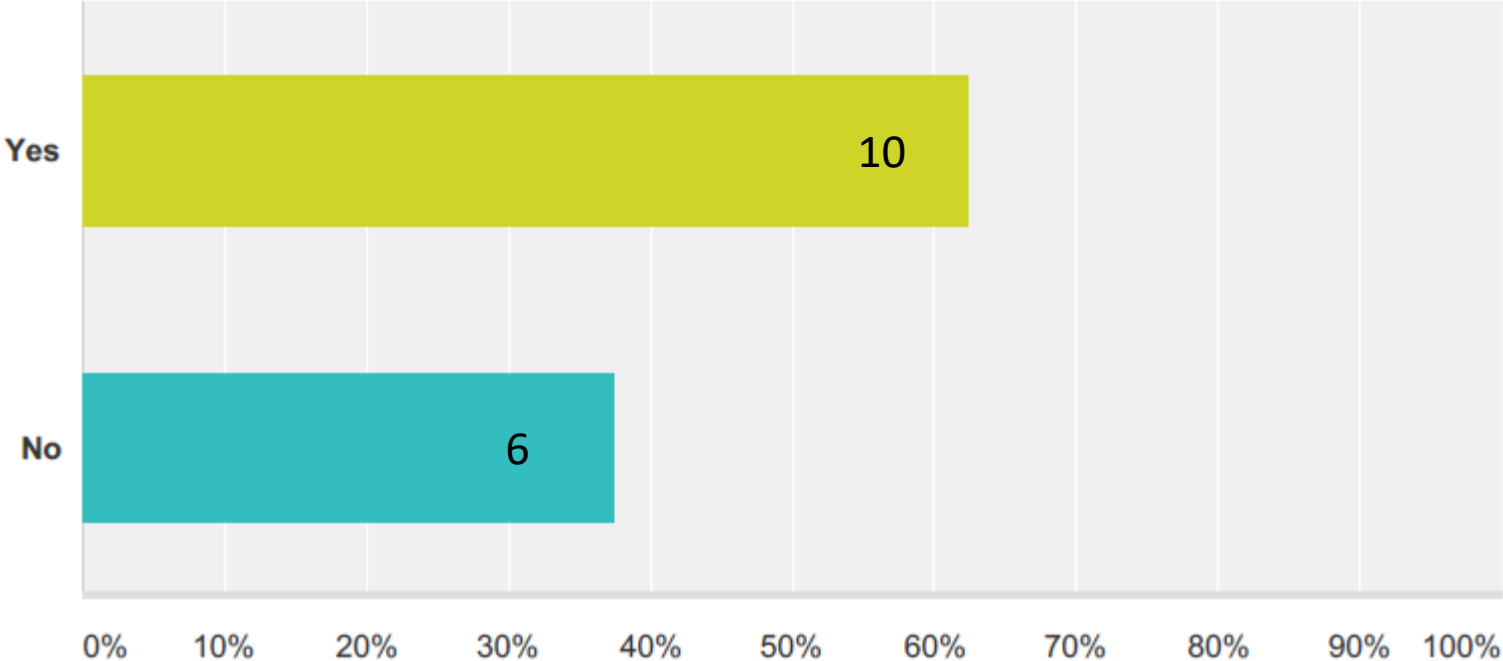


# Modeling in RBPS

- Types of Models
  - At least 9 of the companies who responded are using “typical” ASAP studies and at least 2 are using in house predictive statistical approaches
- MVTR
  - 12 companies reported sometimes utilizing MVTRs in predictions, with the source of the MVTR data split fairly evenly between experimentally derived, default values in software and from supplier information.
  - 5 of these companies also utilized MVTR data and the resulting predictions in regulatory submissions
- What types of things are modelled
  - The majority of responders utilized RBPS approaches to model assay/potency or impurities. Physical attributes such as dissolution, formation of crystalline in amorphous, hardness and color were also modelled.

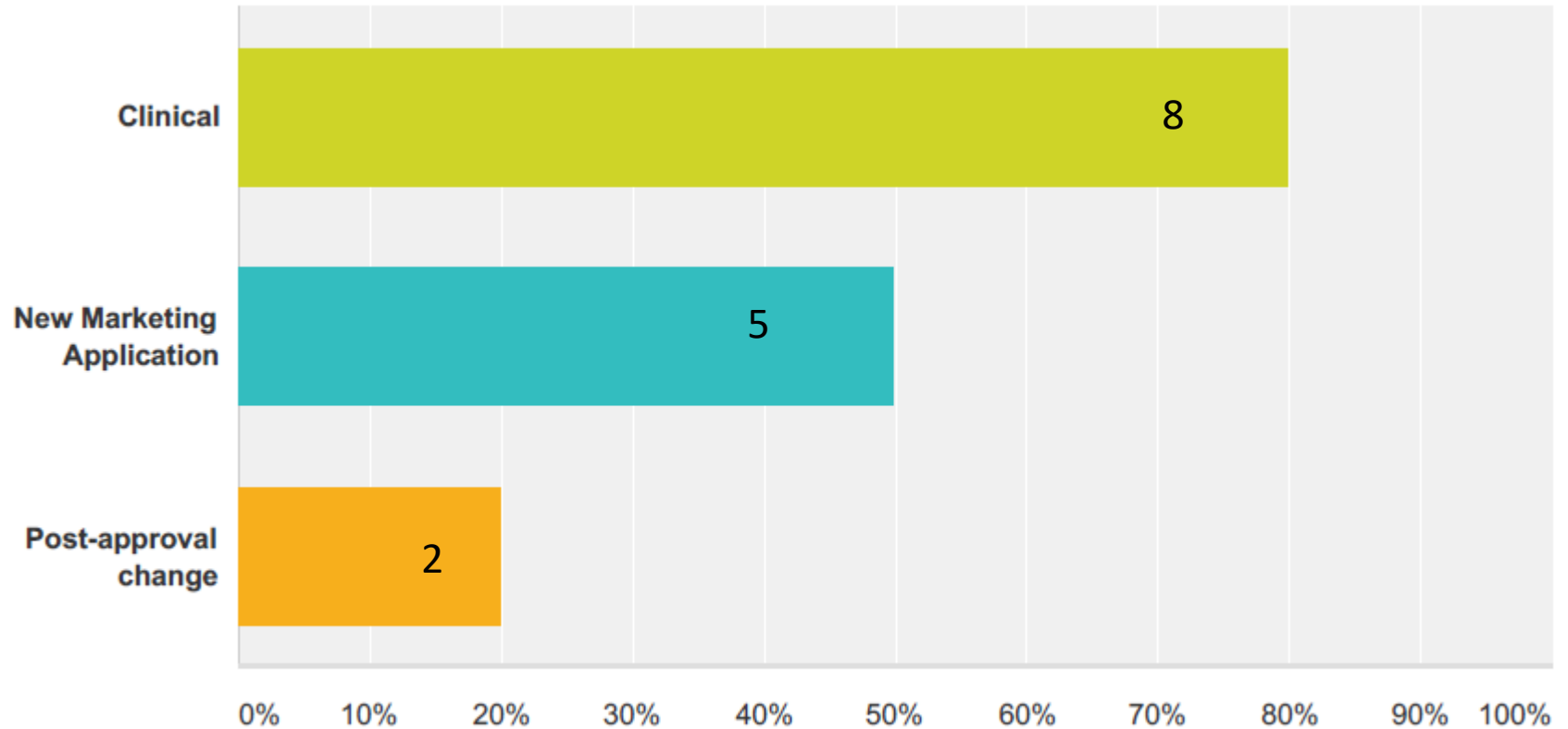
# RBPS is being used in regulatory filings by several companies

**Q9 Has your company used data from risk-based predictive stability studies as part of a regulatory submission?**

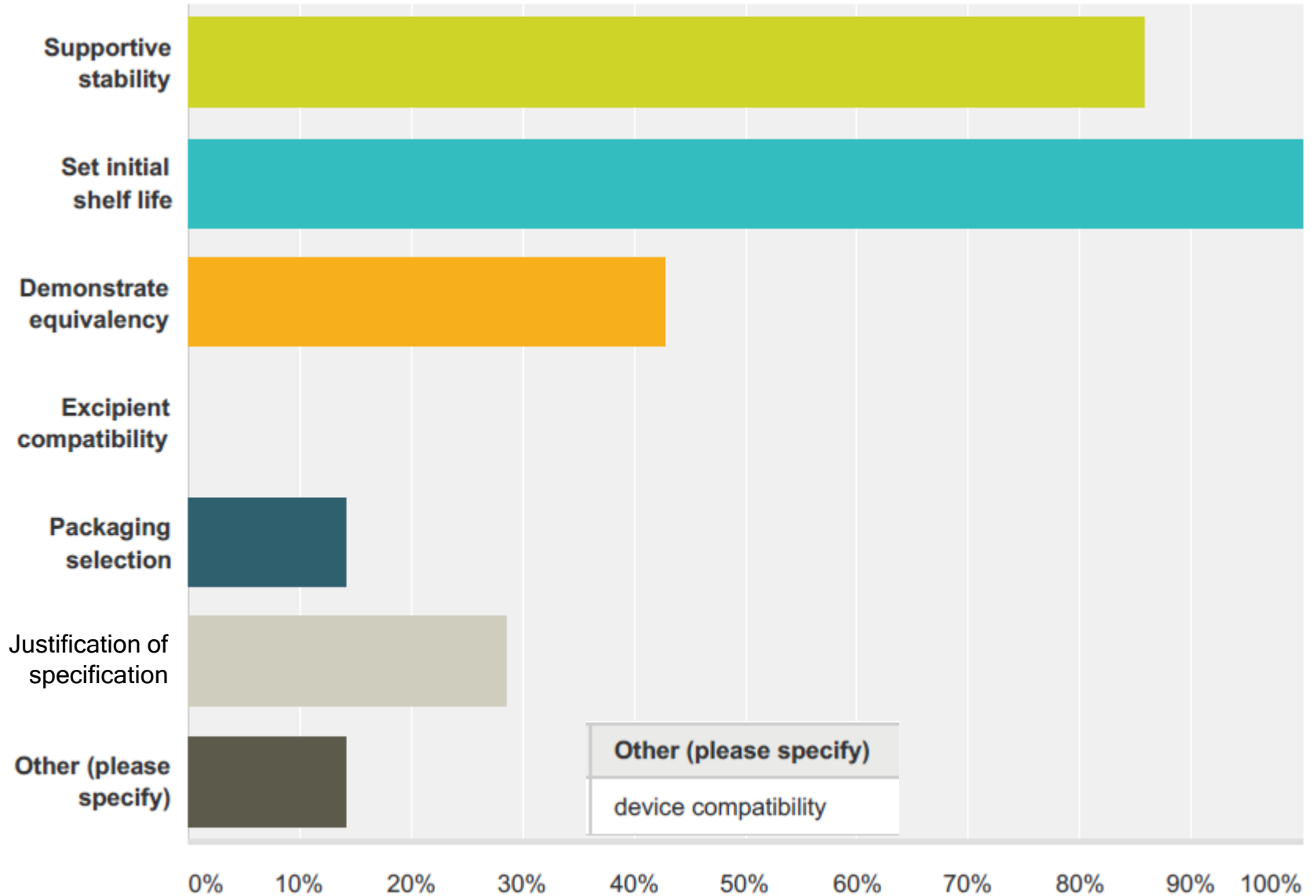




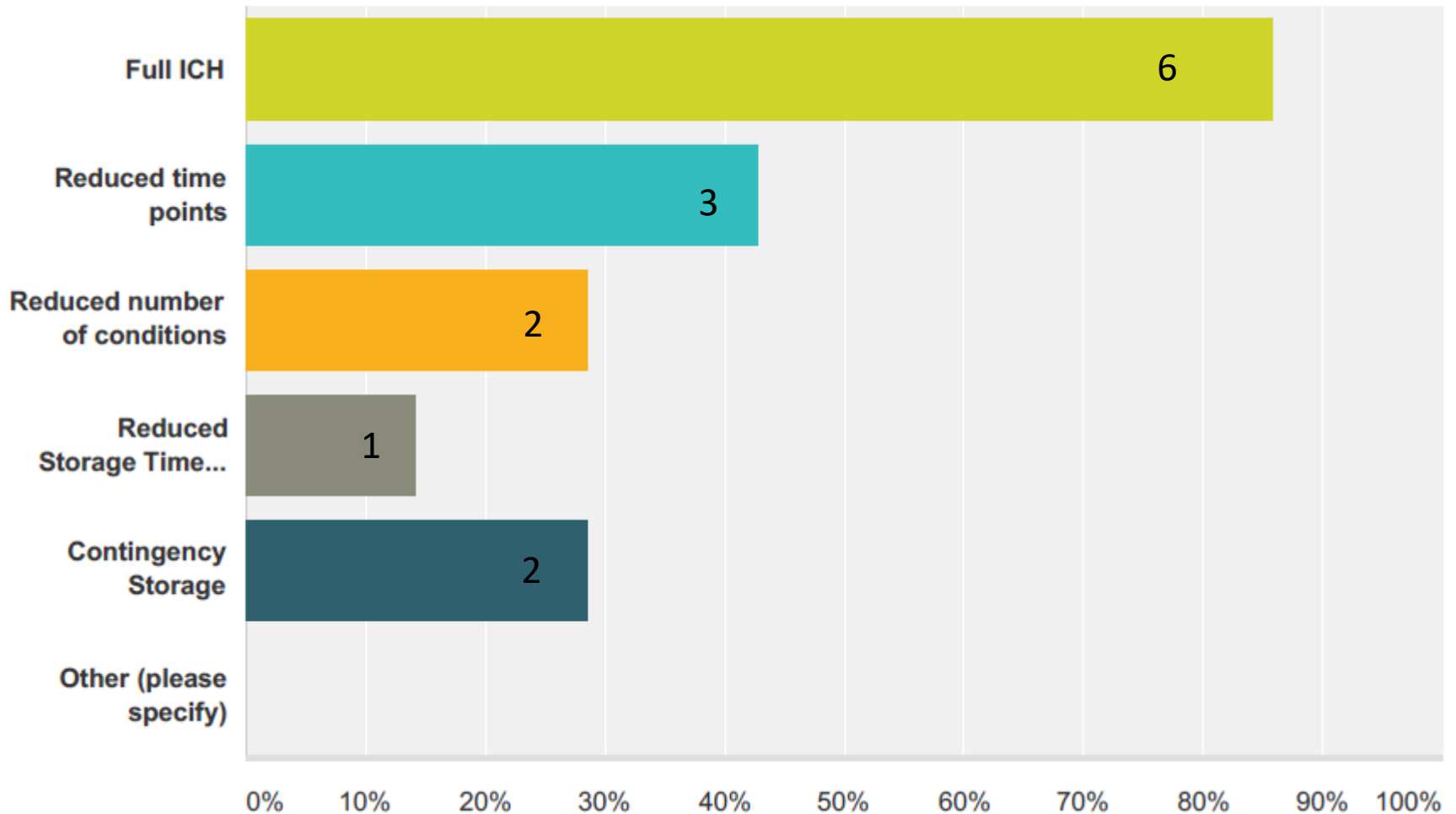
# Regulatory focus of RBPS Primarily Clinical Development



# Regulatory purpose of RBPS in IND/IMPDP filing



# Verifying Results of RBPS in Clinical Development



# Regulatory Experience using RBPS

- Clinical
  - Clinical submissions containing RBPS approaches have been successfully approved in over 23 countries. Countries who did not accept some of these approaches were named as Spain, Czech, France and Italy
- Marketing Application
  - Only 3 companies gave further details of using RBPS approaches in Marketing applications but successful applications “worldwide” were achieved.
- Post Approval
  - One company gave further details of using RBPS approaches Post Approval, to support a packaging change in the USA

# Conclusions

- RBPS is being used by several companies
  - Primarily small molecule
  - Focus on clinical development
- Regulatory experience suggest data has been accepted by many countries
- Limited experience in New Market Applications and post approval changes

# Opportunities

- Ground has been set for broader utilization of RBPS approaches
  - However, based on response, still many companies not working in this space
- More opportunities to utilize in new marketing application/post approval scenarios
  - Tool to understand stability as opposed to simply demonstrating stability
- Some regulators from certain countries refused to accept RBPS approaches
  - Education opportunity
- Several companies still performing full ICH stability to verify RBPS
  - Could this testing be reduced