# Harmonisation: Vision for the Future

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# Why Harmonisation?

- A desire by sponsors to conduct multi-regional trials to support global licensing applications.
- A desire by sponsors to use regional trials to support marketing applications in other regions.
- A desire by sponsors to devote Scientific Advice Meetings to product-specific issues instead of issues related to regional policies and positions.
- A desire for all to have more time to focus on products than to engage in repeated debates.

# All Agree …

- Adaptive design is not a remedy for poor planning. It requires careful planning and rigorous execution.
- It is necessary to proceed cautiously and share experience to advance our collective knowledge.
- It is beneficial to create open forums to hold scientific discussions and to debate in an open-minded manner.
- It is important that the *perfect* does not become the enemy of the *good.*

# Differences Do Exist

- Differences in feedback from different regulators in EU (e.g., sample-size re-estimation, phase II/III trial).
- Differences in feedback from EMEA and the FDA in the US (e.g., DMC, sample-size re-estimation, response-adaptive, inclusion/exclusion criteria, endpoints).
- Differences in feedback from PMDA in Japan and regulators in other parts of the world.

# Vision for the Future

- Based on scientific considerations, regulators across the world hold similar views on the followings:
  - Sample size re-estimation based on nuisance parameters (blinded or unblinded) and treatment effect
  - Role of covariate-adaptive randomization in confirmatory trials
  - Role of adaptive dose-ranging designs
  - Role of homogeneity test in confirmatory trials
  - Situations when phase II/III seamless design is appropriate
  - Situations when sponsor's involvement in a DMC is appropriate

# Working towards the Vision

- Form a world-wide Expert Working Group (EWG) to work through the identified issues.
- The EWG should include all major players involved in clinical trials.
- The EWG produces a global guidance document on adaptive designs.
- Progress the global guidance into an ICH guidance document on adaptive designs.
- Regulators share plans on guidances and actively solicit input from their counterparts when crafting regional guidances. This is taking place in select cases.