Evaluation for Stability data Q1E

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Q1E provides recommendations on :

- How to use stability data generated according to Q1AR

- When and how a retest period or a shelf life can be extended beyond the period covered by long-term data

Q1E contains

examples of statistical approaches to stability data analysis

- Extrapolation
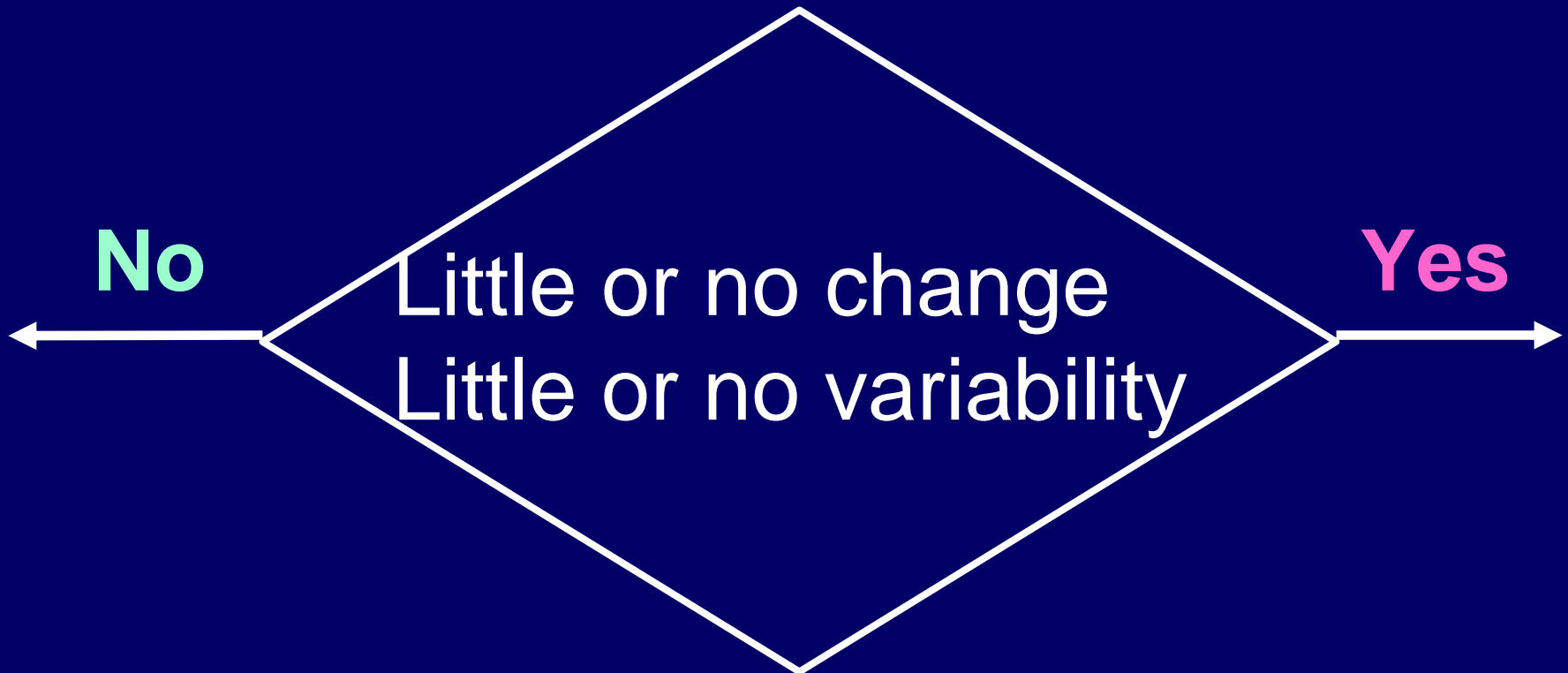
  to extend retest period/shelf life

- Statistical approaches
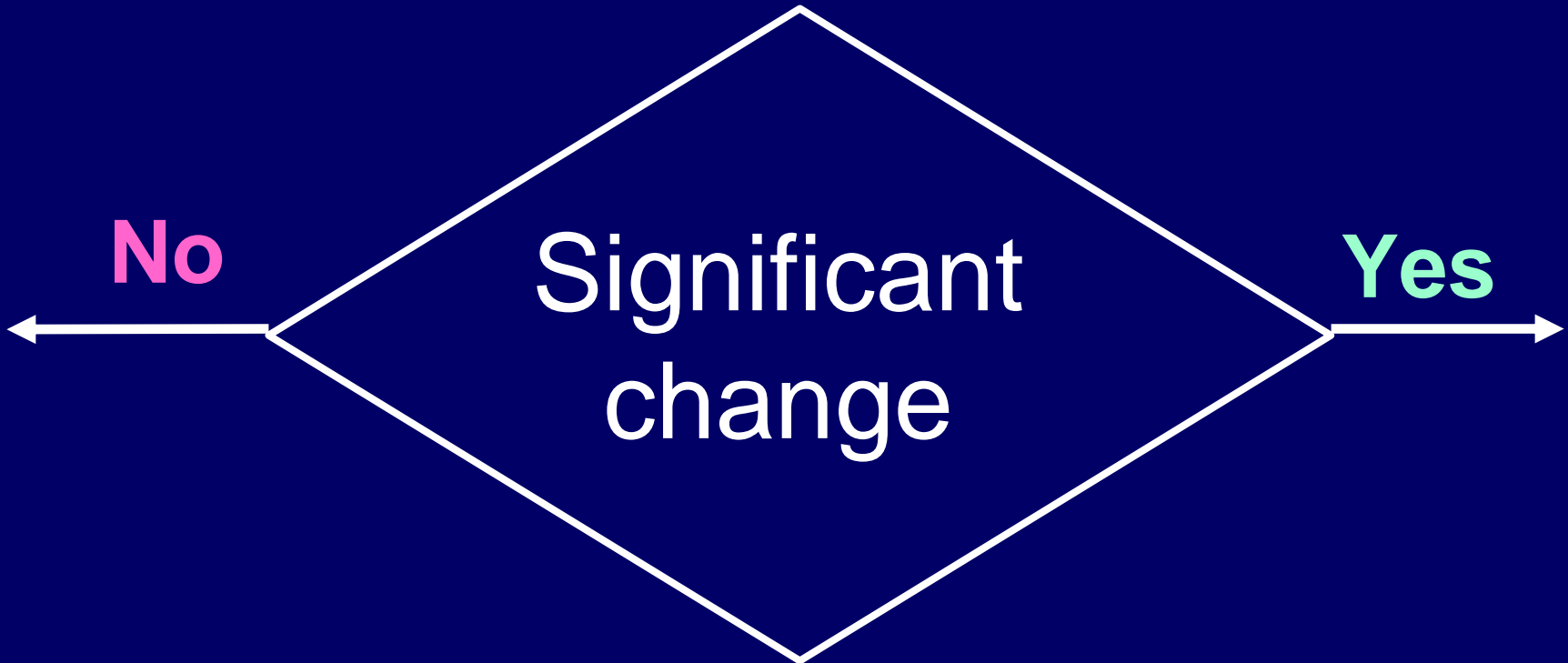
  recommended in the guideline

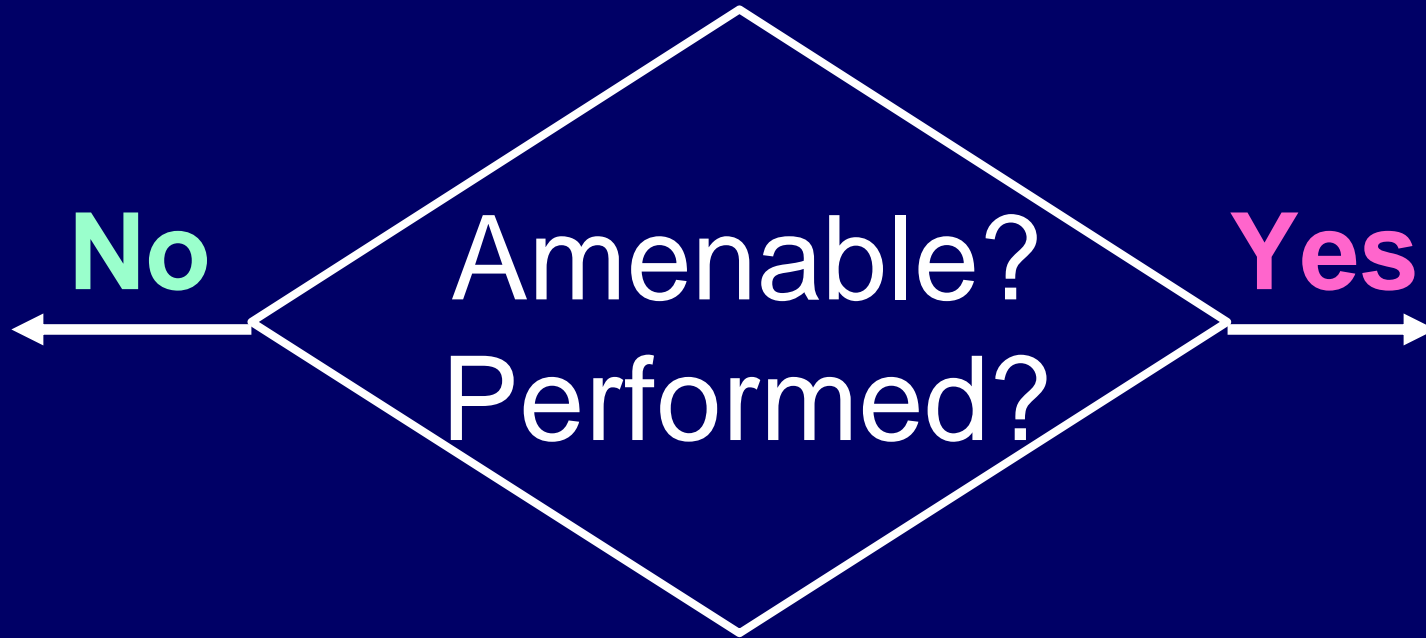**Where no significant change occurs at accelerated condition**

No

Yes

Little or no change
Little or no variability

Accelerated data & Long-term data

Four outcomes
   passing through crossroads
   for Room Temperature Storage

→ **12 month extension**

→ **6 month extension**

→ **3 month extension**

→ **No extension**

Outcome 1   12 month extension

accelerated data show

no significant change

accelerated data & long-term data

little or no change

little or no variability

Outcome 4   no extension

significant change
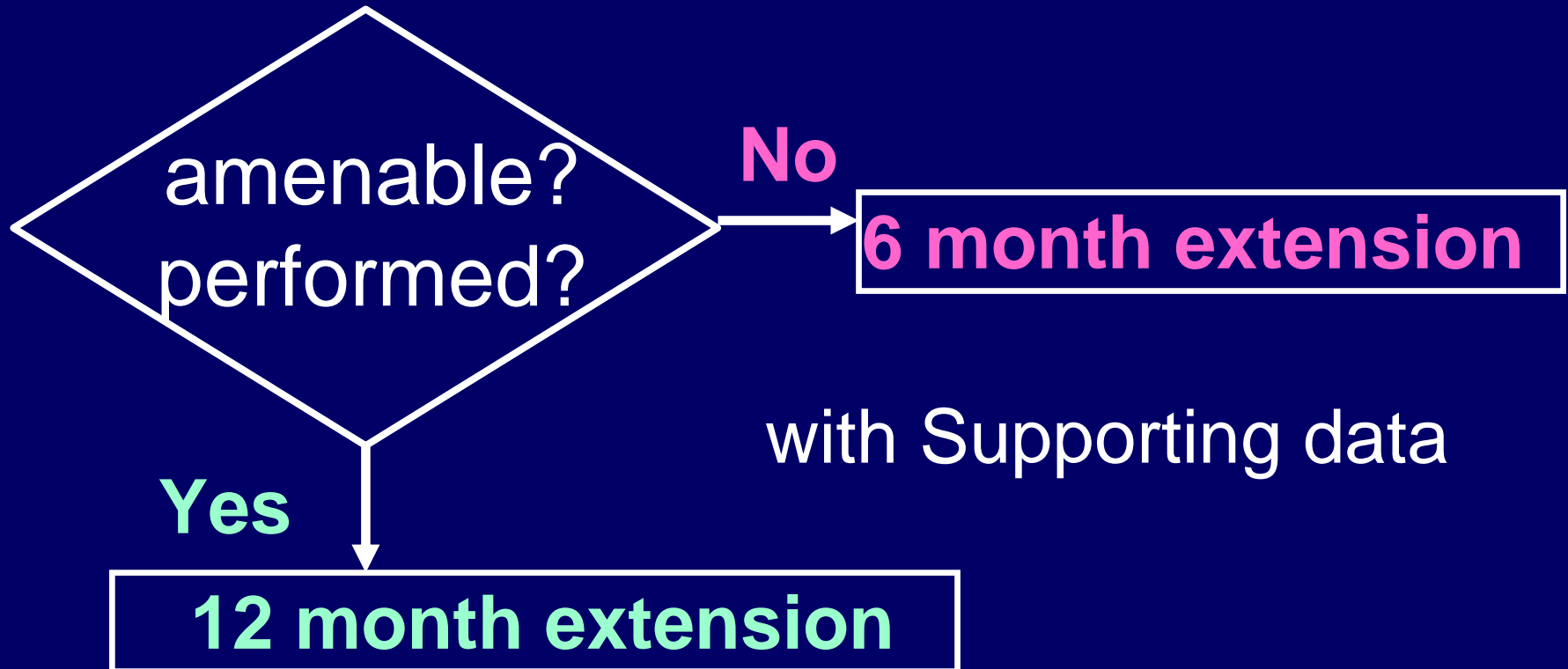
at accelerated condition

at intermediate condition

Statistical analysis

longer retest period/shelf life

(not necessarily required)

Where

- **Accelerated data show no significant change**
- **Changes and variations in accelerated data**
                                                  long-term data

amenable?
performed?

No

6 month extension

Yes

with Supporting data

12 month extension

Where

Significant change at accelerated condition

but not at intermediate condition

amenable?
performed?

No → **3 month extension**

with Supporting data

Yes → **6 month extension**
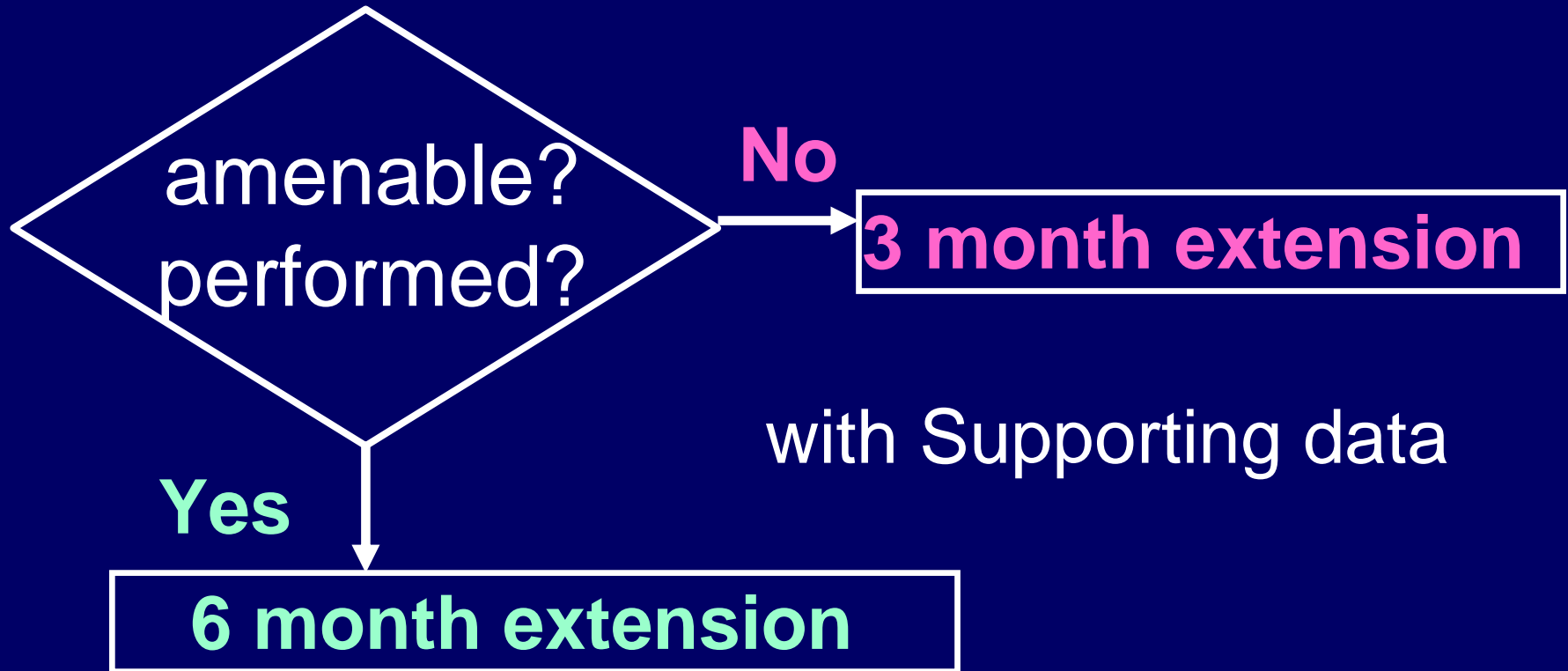
Statistical analysis

longer retest period/shelf life
not always required

Where
- **significant change**
  at accelerated & intermediate conditions
- **variability in long-term data**

→ **Statistical analysis can be appropriate to verify retest period/shelf life**

Statistical approaches
recommended in the Appendix

- **How to analyze long-term data**
  for appropriate quantitative attributes

- **How to use regression analysis**
  for retest period/shelf life estimation

- Examples of statistical procedures
  to determine **poolability** of data from
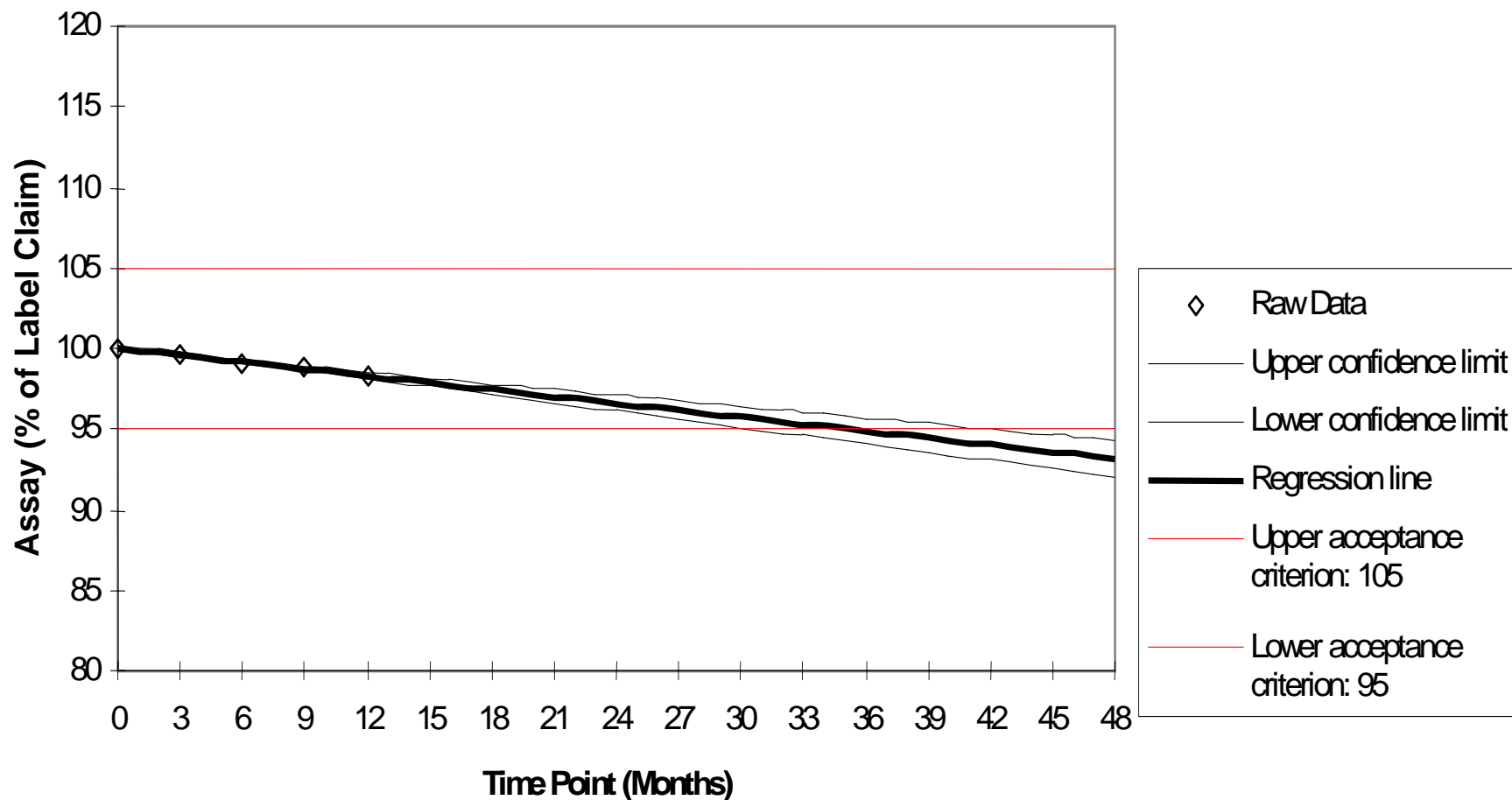 different batches or factor combinations

Regression analysis

Establish retest period/shelf life
with a high degree of confidence

Quantitative attribute will remain
within acceptance criteria
for all future batches

Shelf-life Estimation with Upper and Lower Acceptance Criteria Based on Assay at 25C/60%RH

Statistical approaches
for determining whether data from different batches/factor combinations can be pooled

- **(Approach #1)** Whether data from all batches/factor combinations support the proposed period

- **(Approach #2 "Poolability test")**
  Whether data from all batches/factor combinations can be combined
  for overall estimate of a single period

- **(Alternative approaches)**

Approaches #1 and #2 can also be applied to data analysis for multi-factor studies including Bracketing & Matrixing Designs

Basic Principles

- A shelf life is set based on long-term data

- The extent of extrapolation will depend on accelerated (and if applicable, intermediate) data, as well as long-term data

- Supporting data are useful in predicting long-term stability in primary batches

Basic Principles (cont'd)

- Statistical analysis is not always necessary for setting a shelf life

- A shelf life beyond the period covered by available long-term data can be proposed with supporting data, with or without statistical analysis

- Where a statistical analysis is performed, longer extrapolation can be justified

MHLW Perspective - Q1E

Before Q1E

EU---12 month extrapolation with or without statistical analysis;

US--- max 6 month extrapolation with statistical analysis;

Japan--- no practical extrapolation

- Q1E provides guidance on the extent of shelf life extrapolation in a variety of situations

- Q1E clearly describes the role of accelerated data and of supporting data in shelf life estimation