

# Evaluation for Stability data Q1E

Sumie Yoshioka, Ph. D.

MHLW

National Institute of Health Sciences

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

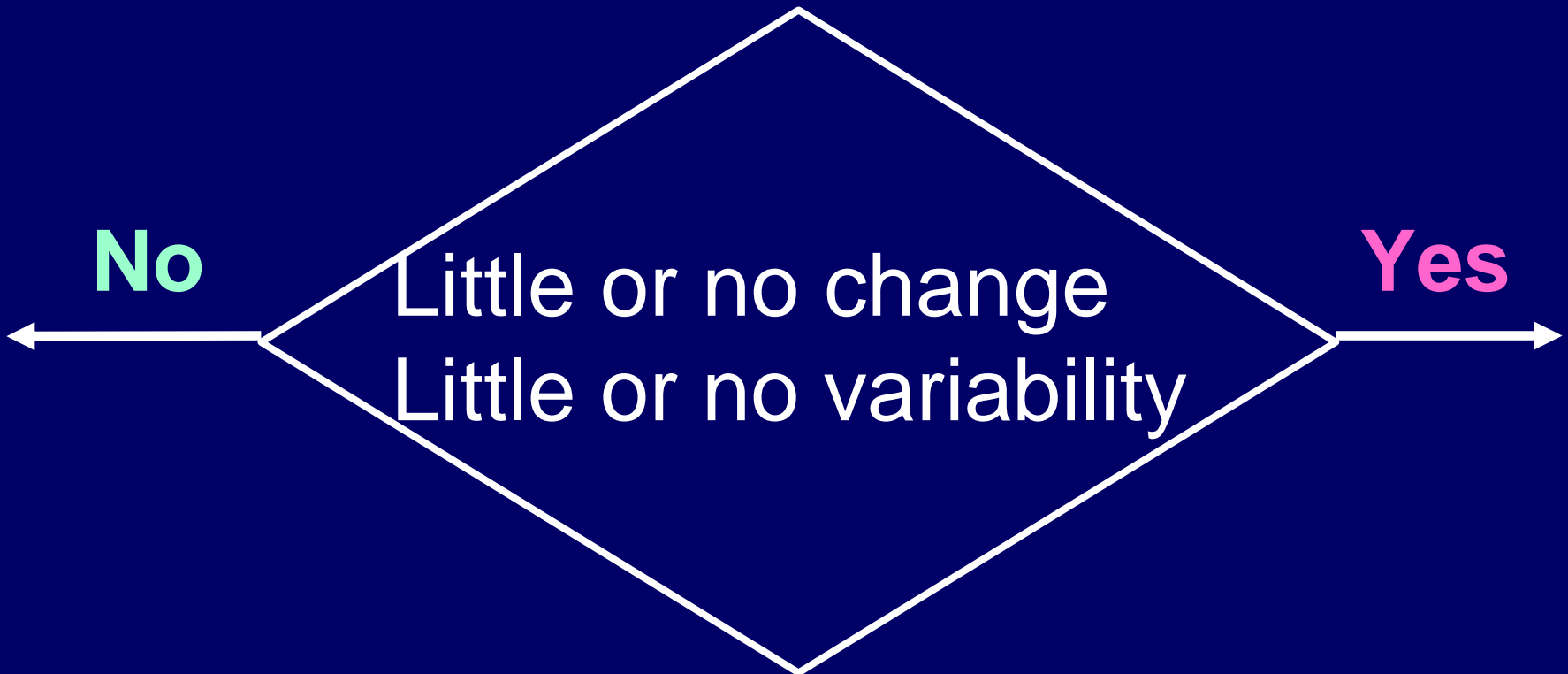
- Statistical approaches

recommended in the guideline



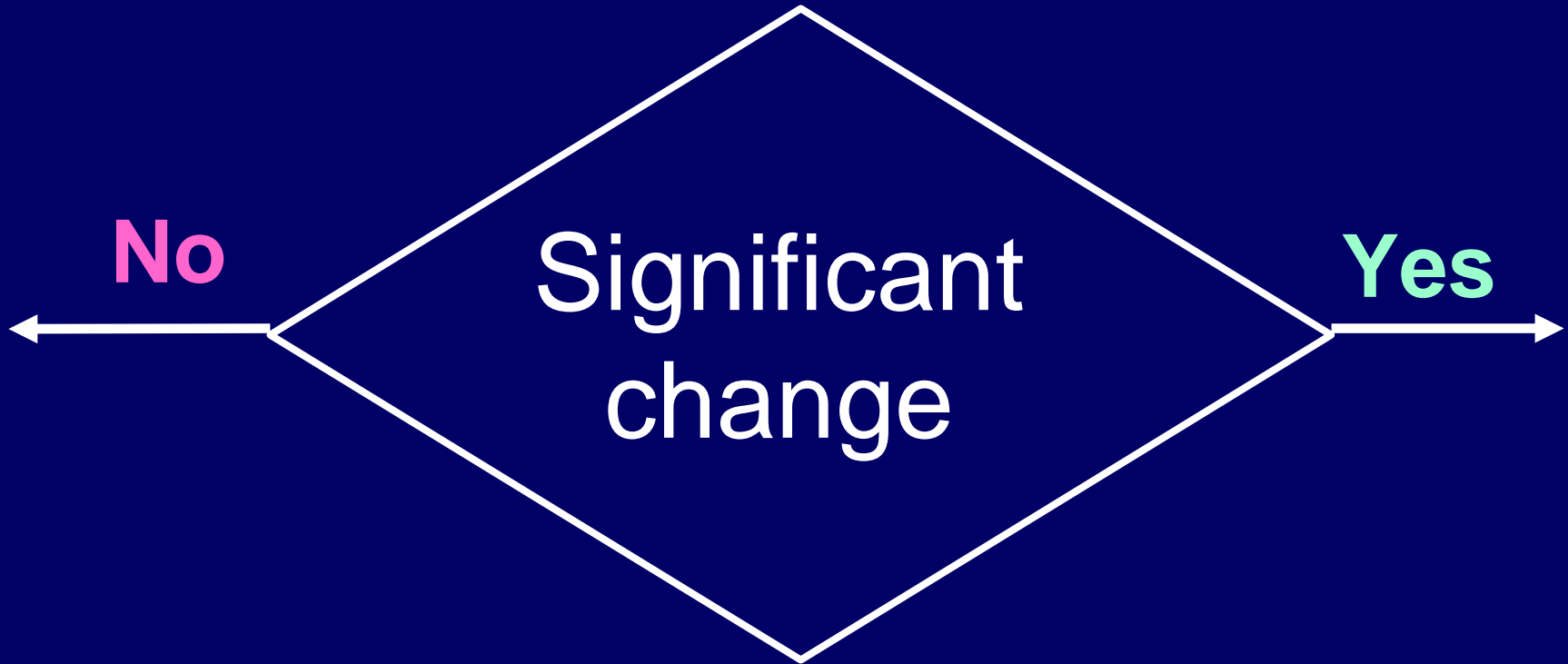
**Accelerated condition**

Where no significant change occurs  
at accelerated condition

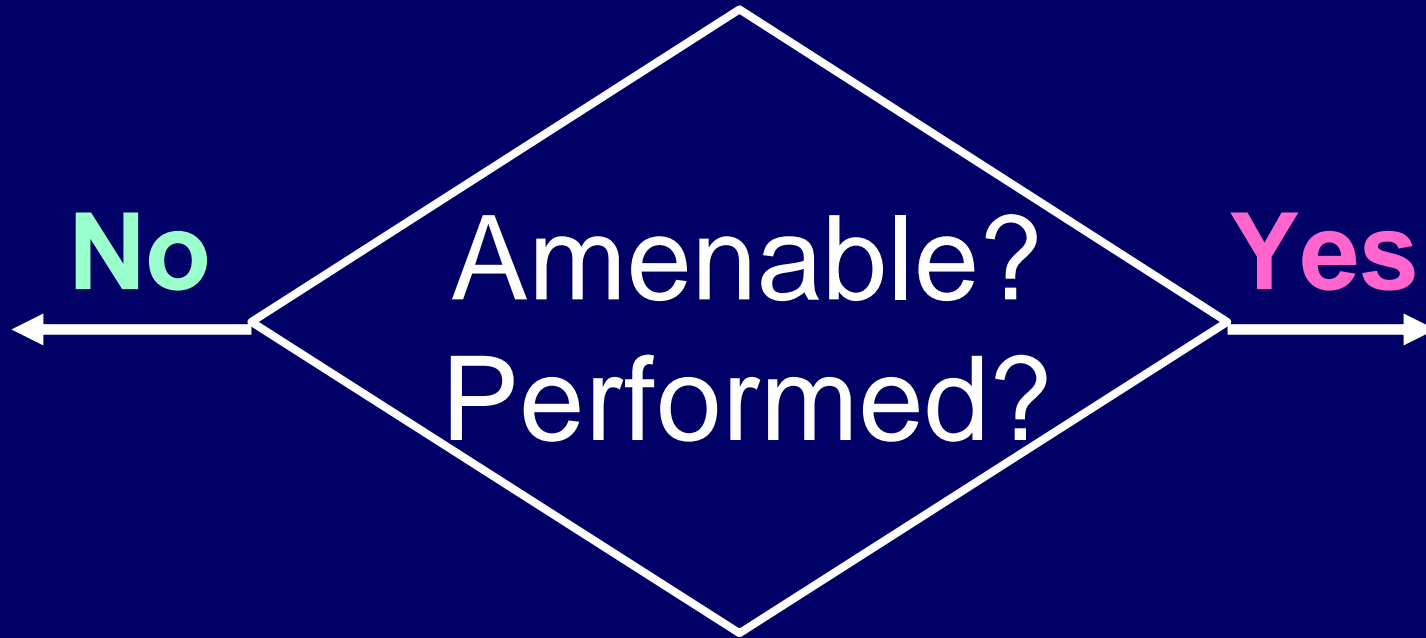


Accelerated data & Long-term data

**Where accelerated data show  
significant change**



**Intermediate condition**



**Statistical analysis**



**Supporting 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

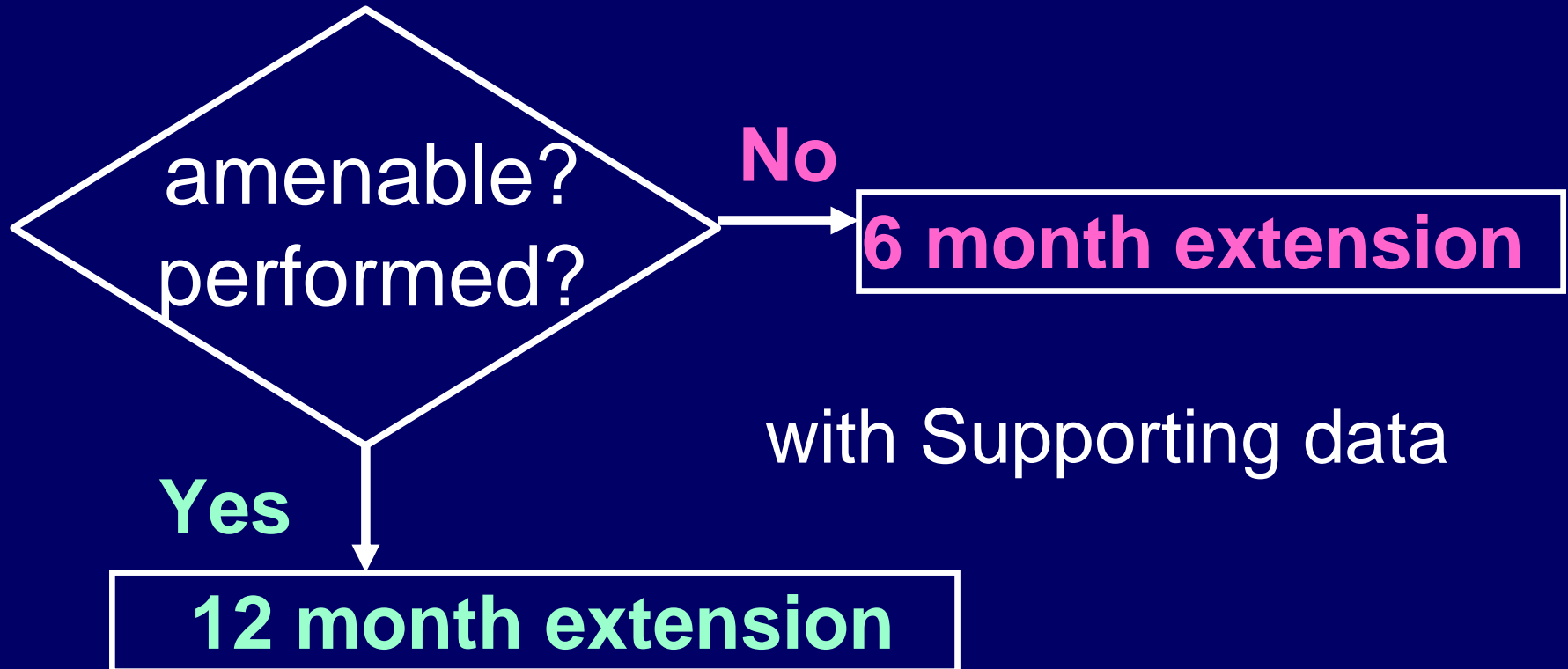
# Statistical analysis

longer retest period/shelf life

(not necessarily required)

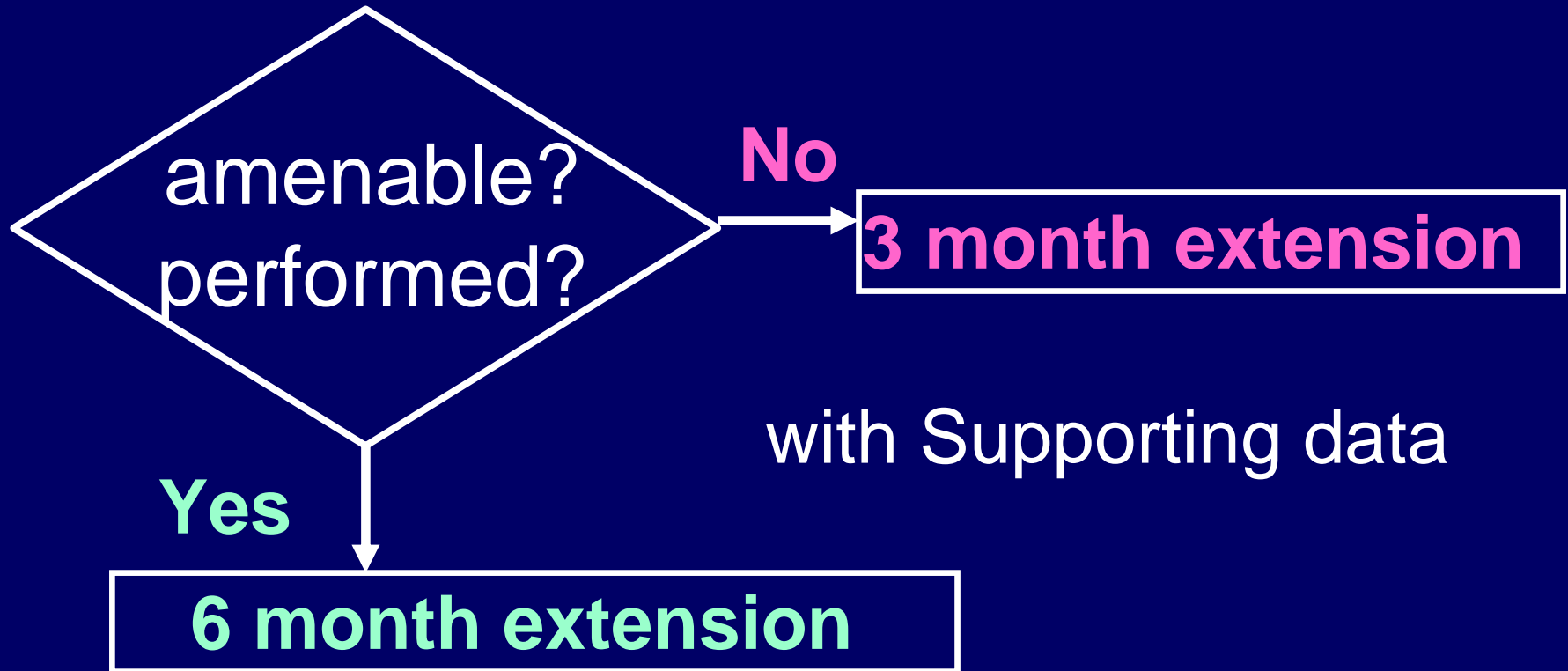
## Where

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



**Where**

**Significant change at accelerated condition  
but not at intermediate condition**



# 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

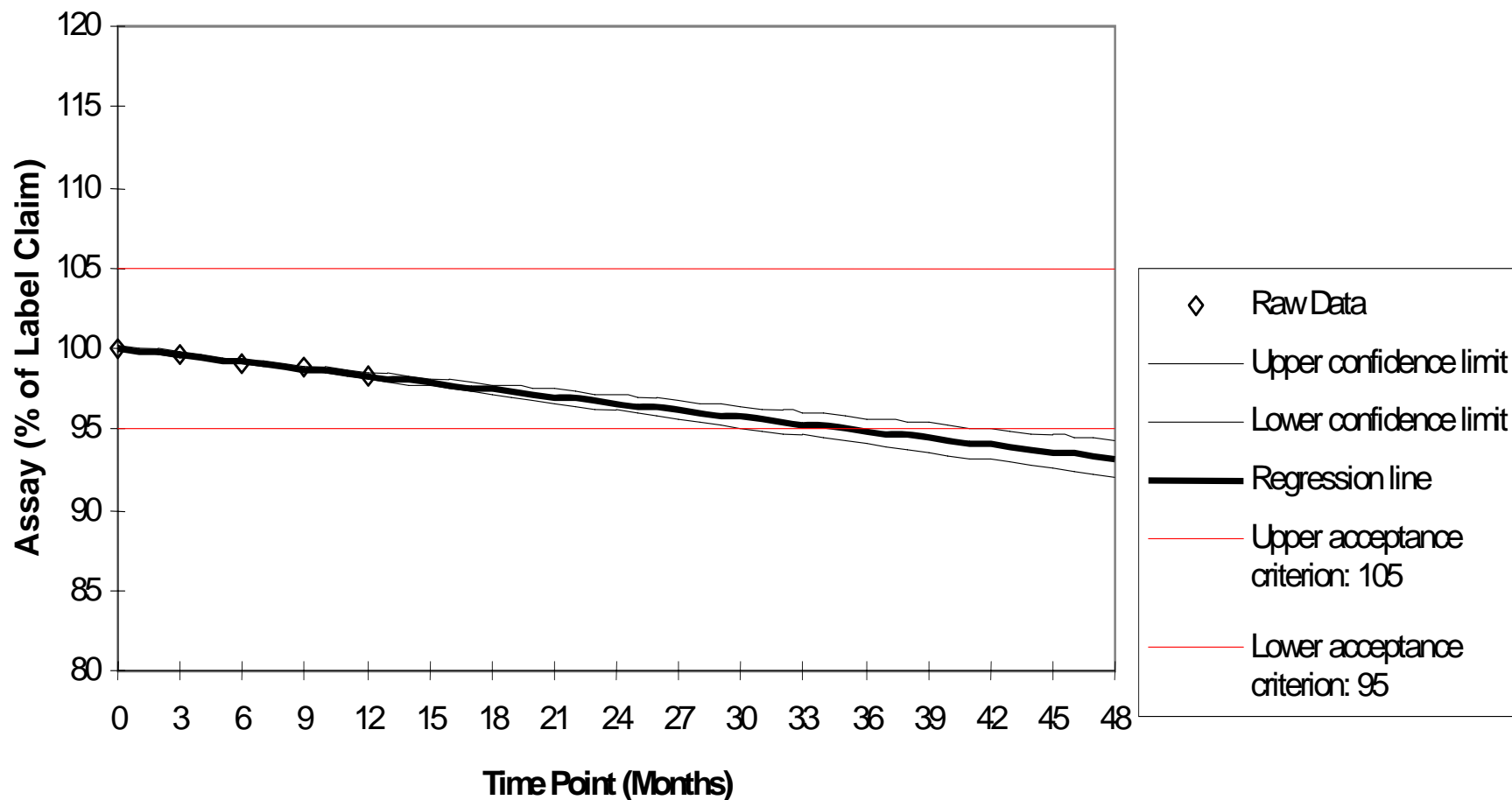
- How to analyze long-term data for appropriate quantitative attributes
- How to use regression analysis for retest period/shelf life estimation
- Examples of statistical procedures to determine poolability of data from different batches or factor combinations

# 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