



# Intelligent stress testing for formulation screening and analytical methods



**A rational and fast stress testing approach with applications in the initial formulation screening and analytical method development and validation**

A. Marangon, U. Bock, E. Haltner

## Introduction

Stress testing or forced degradation studies are an important part of the drug development process and usually are designed to determine the intrinsic stability of the molecule by establishing the degradation pathways in order to identify the likely degradation products and to develop and validate the stability-indicating analytical methods.

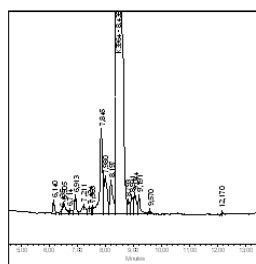
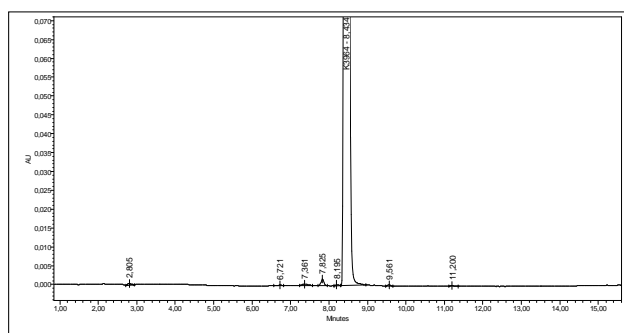
The stress testing is also useful in the preformulation phase during the drug substance and formulations excipients compatibility screening, detecting possible problems since the beginning of the formulation development phase. This

represents a significant time and cost-saving alternative for a drug company.

Across Barriers GmbH designs a range of forced degradation studies oriented and based on results from our Research and Development Group and addresses the investigations to the customer's demand. A dedicated and experienced team combined with our quality assure system in compliance with GLP/GMP guidelines ensures that the required quality standards will be reached.

## Investigation of intrinsic stability of a drug molecule

This test is designed to determine only the stability of the active ingredient, which might undergo different degradation pathways as hydrolysis and oxidation. The test can cover a wide range of pH investigating acidic and alkaline conditions, sensitivity to temperature, humidity and light. A drug stability profile is expected as a result which can be useful in the preformulation phase and development of stability-indicating analytical methods. Across Barriers GmbH offers a rational screening procedure, which perfectly suits if the customer has a large number of drug candidates and desires to obtain a first impression of their chemical stability. In possession of this method, only one milligram of API is required per test condition. The substance degradation profile is reported and the customer receives the result within the period of 10 working days.



## Across Barriers GmbH intelligent stress testing as a time-saving alternative

The advantage of Across Barriers GmbH intelligent screening method in comparison to classical method is the rapid response and release of stability results within few days fitting the demands of the customer schedule. For example, to investigate the compatibility of one active ingredient with twenty excipients, 30 mg of the test substance are required and the results are available in 10 working days.

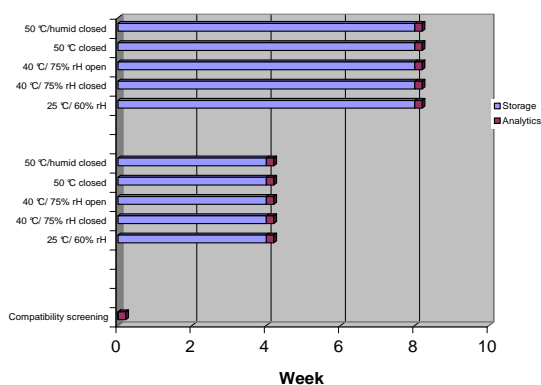


Figure 4: Time comparison between Across Barriers GmbH stress testing and further described classical approaches.

### Service of Across Barriers GmbH: when to apply the stress testing?

- Would you like to develop and validate a stability-indicating analytical method employing a rapid forced degradation approach?
- Are you designing a new vehicle for your drug product and would you like to investigate the substance compatibility with formulation ingredients?
- Do you need to submit stability documentation to regulatory affairs?
- Are you synthesizing new drug molecules and would you like to have an first impression of their stability-pH profile and respective degradation products?
- Would you like to obtain the stability profile and respective degradation products of your new drug with a range of standard excipients?

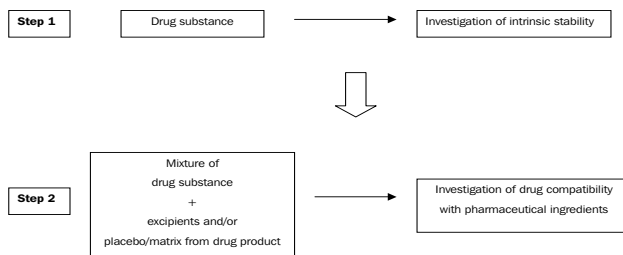


Figure 4: The representative scheme illustrated the different steps during the stress test design.

### Analytical equipments

Across Barriers GmbH offers a range of analytical detection methods including:

- Photodiode array (Waters)
- UV-Vis (Waters)
- Fluorescence (Waters)
- ESI-MS /Micromass ZQ 2000
- ESI-MS/MS /Micromass API
- APCI/ESI-MS Agilent MSD

### Using Across Barriers GmbH intelligent stress testing you minimize time and costs in your development phase.

#### References

- Karen M. Alsante, Linda Martin, and Steven W. Baertschi. A Stress Testing Benchmarking Study. *Pharmaceutical Technology* 2003: 60-72
- Monika Bakshi, Saranjit Singh Development of validated stability-indicating assay methods—critical review. *Journal of Pharmaceutical and Biomedical Analysis* 28 (2002) 1011–1040
- Silke Klick, Pim G. Muijselaar, Joop Waterval. *ess Testing of Drug Substances and Drug Products*. *Pharmaceutical Technology* 2005:48-66
- S. Singh and M. Bakshi, "Guidance on Conduct of Stress Tests to Determine Inherent Stability of Drugs," *Pharm. Technol.* 24, 1–14 (2000).
- ICH Harmonised Tripartite Guideline: Validation of analytical procedures: text and methodology Q2 (R1) step 5. CPMP/ICH/381/95 June 1995
- ICH, *Stability Testing of New Drug Substances and Products*. International Conference on Harmonisation, IFPMA, Geneva, 1993.
- ICH, *Impurities in New Drug Products*. International Conference on Harmonisation, IFPMA, Geneva, 1996.