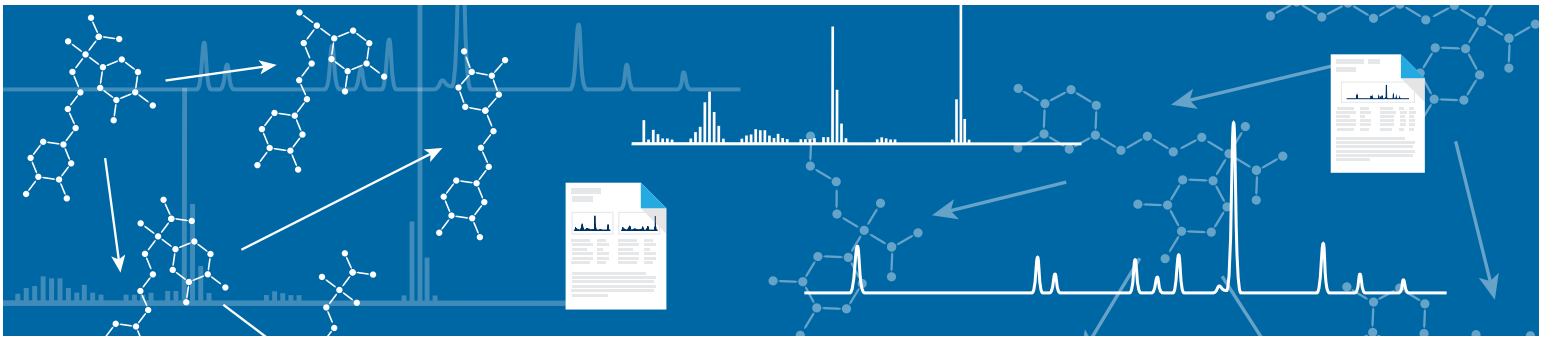
White Paper

An Update for Pharmaceutical Stress Testing Enabled by Modern Informatics Technologies



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ACD/Labs

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I. Introduction

A. Background on Stress Testing

Stress testing or forced degradation is well recognized as a fundamental part of the drug development process, specifically related to purity through control of stability. Control strategies for stability require "stability-indicating" analytical methods, The development and validation of such methods is built on the foundation of well-designed and conducted stress testing studies. The complete regulatory definition of stress testing is found in Q1A(R2).[1] An excerpt of this definition is: "stress testing…can help identify the likely degradation products, which can in turn help establish the degradation pathways and the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedures used." Conditions for stressing include elevated heat and humidity, susceptibility to hydrolysis across a wide pH range, susceptibility to oxidative and photolytic degradation, and in the case of biologics, freeze-thaw cycles and shear (when appropriate).[3] The primary goal is to induce pharmaceutically-relevant degradation pathways in a comprehensive manner, at levels that facilitate stability-indicating analytical method development and validation, such that all realistic degradation products (i.e., those formed during manufacturing, handling, and normal storage and distribution conditions) are formed and can be analytically detected. A more comprehensive list of the objectives of stress testing studies can be found elsewhere.[4-7] The results of stress testing studies are to "…form an integral part of the information provided to regulatory authorities."[6] More recently, there are additional implications for the control of mutagenic degradation products, as outlined by ICH M7.[8]

In the last 20 years much has been written on this topic[4-7,9-15] including two editions of a book devoted to the topic,[6,16] providing helpful guidance on choice of conditions, reasonable endpoints, interpretation of results, and insights into carrying out the studies. This is especially important since the regulatory guidelines are general and do not contain a lot of detail;[17] an exception to this is the legislation and accompanying guidelines[19,20] from ANVISA, where many of the requirements[21] are unique to Brazil.

B. Stress Testing Strategies & Tactics

1. How Strategies Differ through the Various Phases of Development

It is helpful to consider that stress testing is *predictive* in nature, as opposed to definitive. Stress testing is a research tool that is designed to discover potential stability issues with a drug molecule, providing the scientific foundation for developing stability-indicating analytical methods (SAIMs). The use of validated SAIMs for long-term stability studies provide the definitive stability information. A representation of the overall strategy is shown in Figure 1.

Typically, stress testing is not a "one time" event;[22] rather it is performed at several stages in the "life cycle" of a novel drug candidate with different goals, strategies, and levels of thoroughness. The regulatory guidance of the FDA does not explicitly require stress testing to be performed or reported during Phase 1–2 stages, although it is encouraged

to facilitate the development of stability-indicating methods.[23,24] The FDA guidance does require drug substance stress testing for Phase 3 and suggests these studies be conducted on drug products as well. For the New Drug Application (NDA), the guidance requires a summary of DS and DP stress studies including elucidation of degradation pathways, demonstration of the stability-indicating nature of the analytical methods, and identification of significant degradation products.[25,26]

From an industry point-of-view, it is the failure rate of new drugs during clinical development that drives the strategy for conducting stress testing as a function of the development timeline. Current estimates are in the realm of 5–10% success when evaluated from the decision to take a drug into the clinic through regulatory approval. Thus, postponing the most thorough (and therefore most expensive) studies for late phase development, while ensuring stability and safety for the shorter and more controlled environment of early clinical development, is the strategy for most companies.[27]

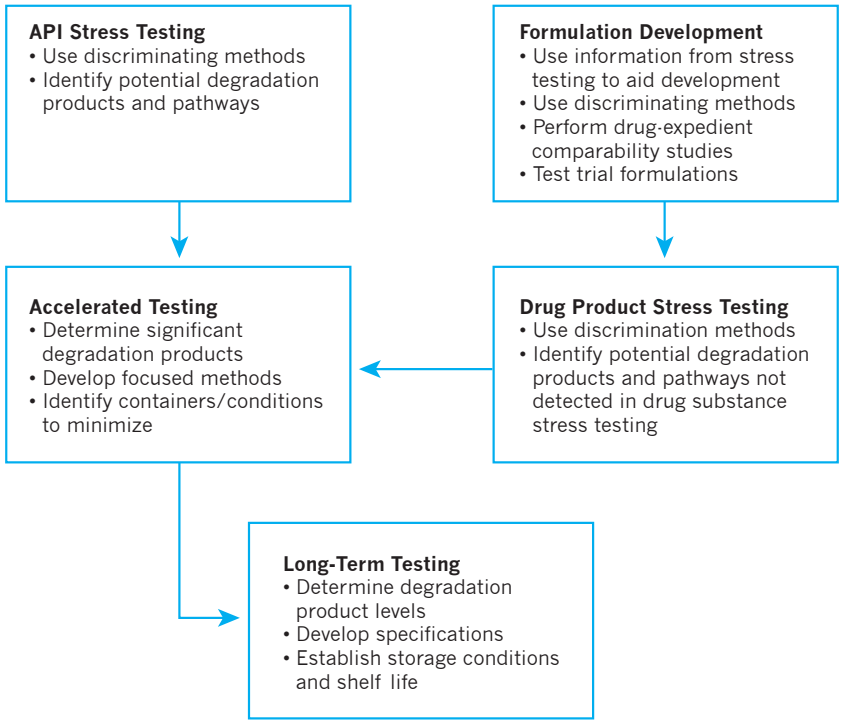


Figure 1. Relationship of stress testing in the overall strategy for prediction, identification, and control of stability-related issues.

2. Implementing Stress Testing Methods—the Tactics

A stress testing process flow map (Figure 2) has been proposed by Alsante *et al.*[5,7] involving 8 steps (step 4A has been added by the author). The first step involves prediction of possible or likely degradation products (e.g., using chemistry principles, knowledge of the molecular scaffold, literature, and available *in silico* tools). Combining these predictions with additional information (pK(s), known chemical stability/degradation products, previously established analytical methods, hygroscopicity, solubility, etc.) a protocol can be designed for the appropriate stress conditions and experimental set up, and the experimental protocol can be carried out in the laboratory.[28] The stressed samples are then analyzed using suitable analytical methodology as an initial screen; subsequently

the methodology can be revised or optimized (e.g., using HPLC screening protocols[29,30] or computational tools such as DryLab™, ChromSword, or AutoChrom™), and the method can be validated as appropriate. Purity, potency, relevant kinetics, and mass balance can be derived from analysis using the optimized method, and the major[31] degradation products (labeled "KPSS" for "Key Predictive Sample Set" in Figure 2) can be flagged for further tracking (e.g., peak tracking using PDA-UV-Vis and/or MS) in other partially-degraded stress samples, as well as in other stability samples.

Mass balance in partially degraded samples is an important aspect of a complete understanding of the major/relevant degradation pathways, but it often proves challenging to assess accurately. Mass balance is often calculated by simply evaluating the summed peak areas of all degradation products and the parent drug and comparing the total area to an un-degraded (or initial, unstressed) sample. For a method using HPLC with UV detection, such an approach is an assessment of the "chromophoric" mass balance; without knowledge of the relative response factors of individual degradants, the results may or may not reflect true mass balance. A fishbone diagram has been developed for the causes of mass imbalance (Figure 3); for more thorough discussions of this important topic see Baertschi *et al*.[32]

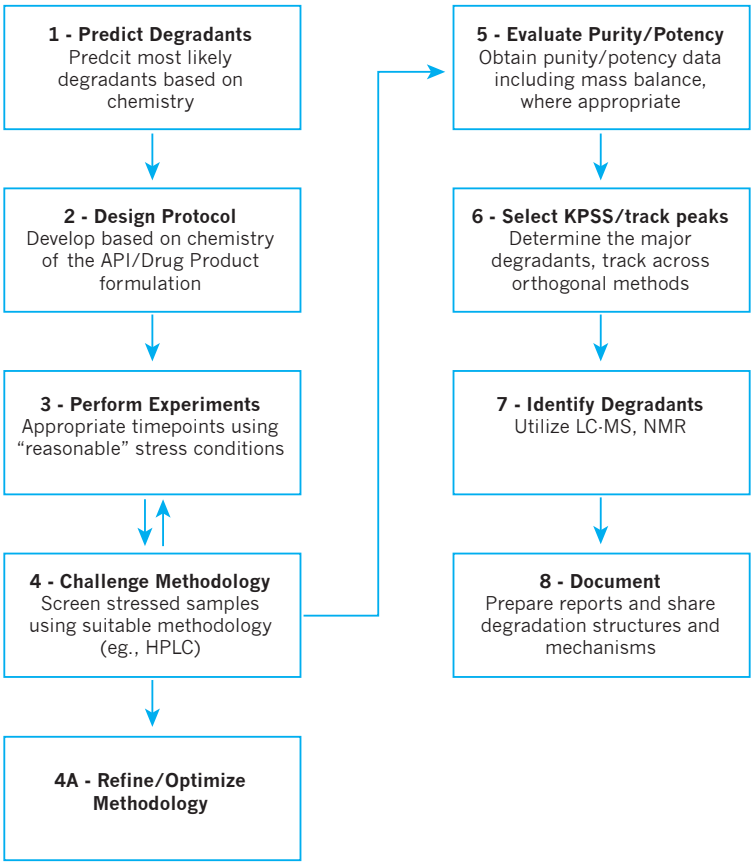


Figure 2. Forced Degradation Process Flow Map Proposed by Alsante *et al*.[7] Note: KPSS = key predictive sample set, the set of conditions/time points that contain all major degradation products. The KPSS is used to develop the analytical methodology with appropriate resolution and detection limits.

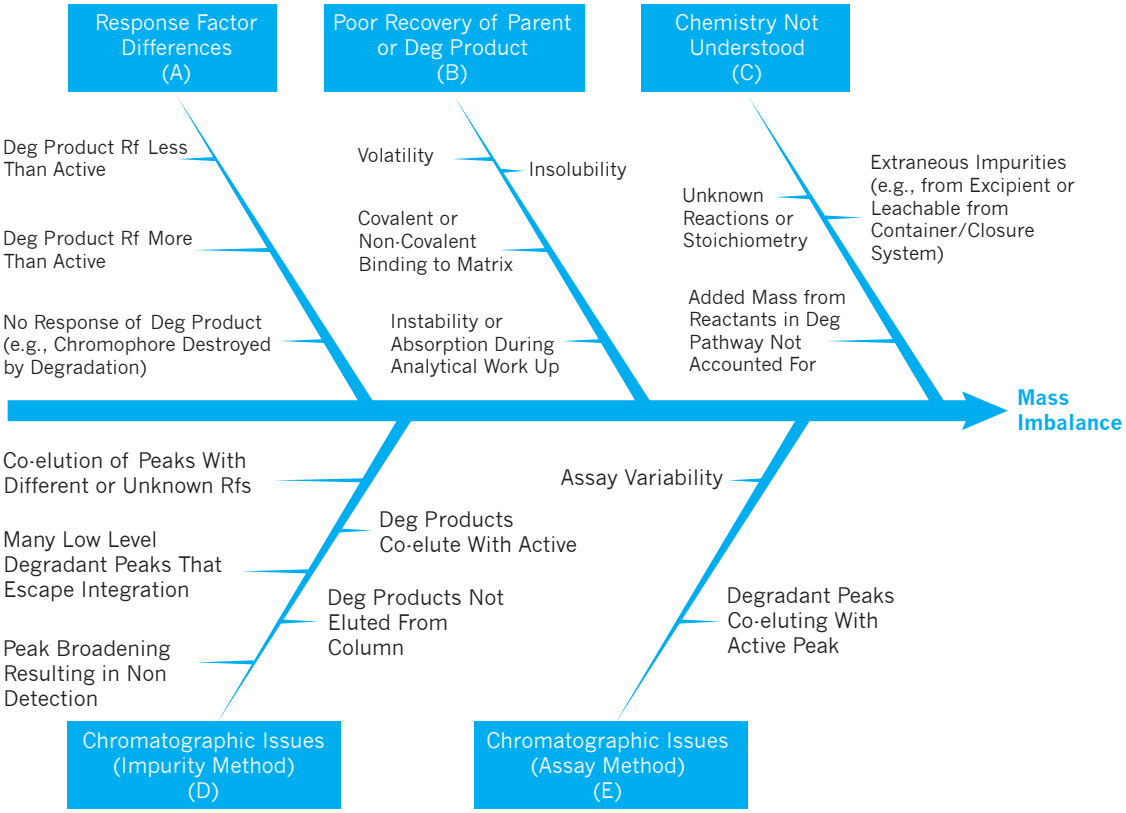


Figure 3. Fishbone diagram of the major causes of mass imbalance.[32]

The next step to consider is structure elucidation of the major degradation products as part of establishing the degradation pathways and developing an understanding of what parts of the molecule are susceptible to degradation by the various stress conditions. Finally, all parts of the study need to be documented in reports that capture the information and knowledge gained in a meaningful and retrievable way.

II. Why is an Update Necessary? Enabling Technologies

If stress testing is well-developed, thoroughly and well-described in the literature, as could be inferred from the Introduction section, what is the purpose of this current paper? Why is an update on the topic needed and/or relevant? What has changed?

First, while much has been written about stress testing, it has been referred to as an "artful science",[6] a "gray area"[9] that is a research undertaking on diverse molecular entities, requiring significant flexibility in the design and execution in order to obtain appropriate and relevant results. This is one of the reasons that **the field still does not have widespread consensus** on various aspects of such studies, e.g., on specifics of the conditions of stressing, execution of studies, interpretation of results, and whether or not to identify degradation products observed.

Second, and relevant to the purpose of this paper, **tools are continuing to develop** that enable the various steps outlined in Figure 2. For example, tools to help (a) guide the

protocol design through theoretical predictions, (b) design and optimize chromatographic separation and detection, (c) elucidate structures of degradation products, (d) track degradation product peaks, and (e) prepare meaningful and retrievable reports that can facilitate decision-making and cross-functional collaboration.

A. Guiding Design Through Predictions

1. pK_a Prediction

A fundamental but often overlooked aspect of understanding the degradation chemistry of a drug is the protonation state of the molecule under the various conditions of stress. Experimental measurements of pK_a values are typically made using potentiometric or UV/Vis-titrations,[33] with other techniques available (e.g., NMR, conductometry, fluorescence spectroscopy, voltammetry/polarography, and infrared spectroscopy[34]); such measurements can usually provide definitive values for the various pK_a values in a molecule, if the molecule is ionizable. Before such data are available, however, theoretical predictions can readily be obtained using a variety of available tools.[35] Standard methods for pK_a prediction can be classified into two major groups: empirical methods and quantum chemical methods. Such theoretical predictions are typically quite good, with the top performing methods being empirical methods. Interestingly, the ACD/pK_a DB tool performance was in the top three, and arguably the best overall predictor for pharmaceutical drug substances in one published study.[36]

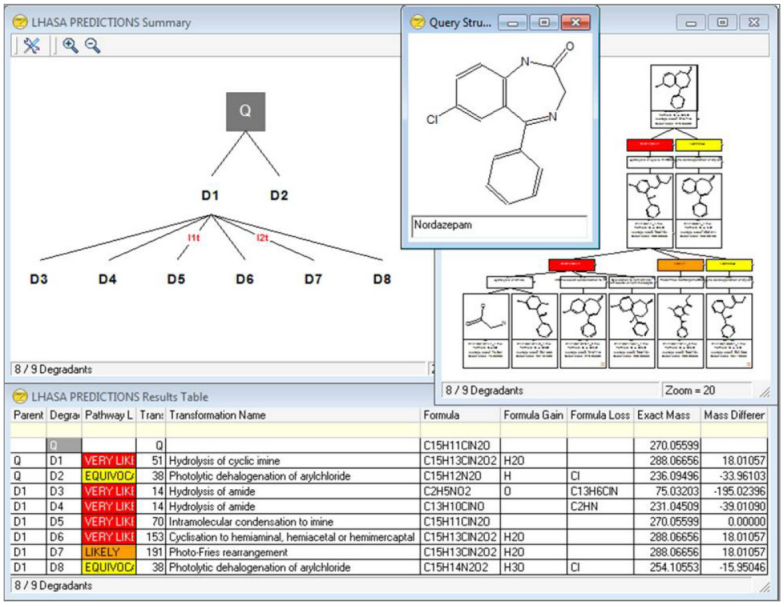
2. Theoretical Degradation Pathway Prediction

The first approach for predicting theoretical degradation pathways/products is to consult the literature, internal company information, the drug master file, or relevant pharmacopeias, for information describing the known chemistry associated with the compound. If no drug-specific knowledge is available, analogous information on similar molecular scaffolds, combined with organic chemistry principles, can lead to theoretical products and pathways.

Organic chemistry principles alone can also be used to propose theoretical degradation chemistry; however, it can be difficult for even an experienced degradation chemist to keep up with the rapid development of such knowledge, let alone a fast and full recall, piecing together such knowledge in an objective way to assemble various possible products and pathways. Computerized approaches have developed rapidly over recent years, leading to dramatic increases in various *in silico* predictive capabilities. As noted elsewhere,[37] there are two *in silico* approaches available: logic-oriented and information-oriented. While logic-oriented systems use mathematical/quantum mechanical models to search for possible solutions to the query, information-oriented systems, often called expert systems, attempt to emulate the decision-making process of a human brain by accessing a "library" or knowledge base of known information (which can be updated as new information is developed or becomes known).

Zeneth™,[68] is an information-oriented *in silico* tool, developed specifically for the prediction of forced degradation pathways; it is currently the only "commercially available and actively maintained"[37] program for this purpose. It was designed as part of an industry-consortium with Lhasa Ltd to predict theoretical degradation pathways of a molecule

based on its structure and user-selected conditions and processing constraints. The program can also predict potential degradation reactions with counterions and excipients (and commonly associated impurities in excipients), expanding the capabilities into formulated products. The performance of the consortium-based Zeneth software continues to improve through industry feedback and active development by Lhasa. Zeneth provides output in reports in a proprietary file format, Excel, Word, and SDfiles.



Parent	Degra	Pathway L	Trans	Transformation Name	Formula	Formula Gain	Formula Loss	Exact Mass	Mass Differer
	Q		Q		C15H11ClN2O			270.05599	
Q	D1	VERY LIKI	51	Hydrolysis of cyclic imine	C15H13ClN2O2	H2O		288.06656	18.01057
Q	D2	EQUIVOCA	38	Photolytic dehalogenation of arylchloride	C15H12N2O	H	Cl	236.09496	-33.96103
D1	D3	VERY LIKI	14	Hydrolysis of amide	C2H5NO2	O	C13H6ClN	75.03203	-195.02396
D1	D4	VERY LIKI	14	Hydrolysis of amide	C13H10ClNO		C2HN	231.04509	-39.01090
D1	D5	VERY LIKI	70	Intramolecular condensation to imine	C15H11ClN2O			270.05599	0.00000
D1	D6	VERY LIKI	153	Cyclisation to hemiaminal, hemiacetal or hemimercaptal	C15H13ClN2O2	H2O		288.06656	18.01057
D1	D7	LIKELY	191	Photo-Fries rearrangement	C15H13ClN2O2	H2O		288.06656	18.01057
D1	D8	EQUIVOCA	38	Photolytic dehalogenation of arylchloride	C15H14N2O2	H3O	Cl	254.10553	-15.95046

Figure 4. Example of the output from the chemical degradation prediction program Zeneth. Results are for nordazepam for pH 1, water, and light stress conditions. Q is the query compound (the drug of interest) and D(n) are the degradation products. (Figure adapted from ref 38.)

3. Other Computational Chemistry Tools

The use of logic or semi-empirical/quantum mechanical calculations to study or predict drug degradation pathways has not been systematically or extensively developed, although some studies have been published.[39,40] It remains to be seen whether such calculations will become broadly used tools for degradation studies; as computers become faster and more powerful, and algorithms are further developed, the possibilities may translate into reality. The computational approach that has been studied the most is the susceptibility of drugs (or other compounds) to autoxidation (radical-initiated oxidation) via calculation of the bond dissociation enthalpies (BDEs) of hydrogen-atom abstraction (to form a radical within the drug of interest).[41,42] Such methods are reasonably well-developed and can provide useful and predictive results for which sites of a molecule are most susceptible to radical-initiated oxidation. A risk-scale correlation of calculated BDEs vs. experimental has been published, and a figure from the publication is shown in Figure 5.[42] Deducing the degradation products that would result from H-atom abstraction, however, requires additional insight that derives from chemical principles and degradation chemistry knowledge.

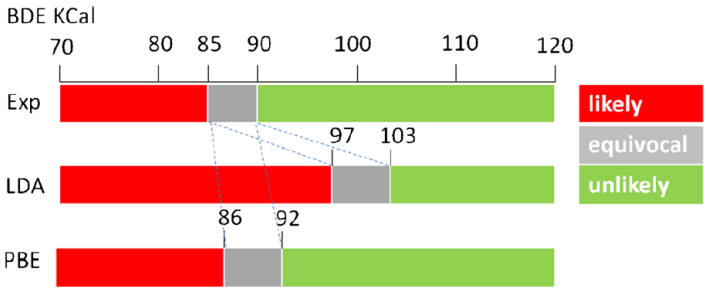


Figure 5. Risk scale for H-atom abstraction via radical-initiated oxidation (reproduced from ref 42). Correlation of experimental results to calculated bond dissociation enthalpies aids interpretation of calculated results.

4. Mutagenicity Prediction

The ICH M7 guideline describes the process for identifying actual and potential impurities likely to be present in the drug substance and product in the context of performance of risk/hazard assessments. For impurities that have been structurally-identified, when adequate experimental mutagenicity and/or carcinogenicity information is not available, a structure-based computational toxicology or quantitative structure activity relationship [(Q)SAR] analysis, using two complementary approaches (i.e., expert rule-based and statistical-based) may be used to predict the mutagenic potential of an impurity, including the assignment into one of five hazard classifications. The principles and procedures for conducting (Q)SAR analyses in alignment with ICH M7 have been described,[43] as well as the predictive performance of such tools.[44,45] The difficulty for degradation product mutagenicity risk assessment is that the evaluation process must include projections about which products will form over the shelf life of the drug substance and product. An overall process flow for such assessments has been proposed.[46]

While theoretical predictions of the potential of a particular drug to form mutagenic degradation products can be made based on chemical principles[47] or software like Zeneth, a significant difficulty for making decisions about inclusion of degradation products in (Q)SAR screening is the "likelihood" of formation, i.e., which products will likely form (above the certain thresholds) over the shelf life of the DS and DP. As discussed by Kleinman *et al.*,[46] ICH M7 states that "actual and potential degradation products likely to be present in the final drug substance or drug products and where the structure is known should be evaluated for mutagenic potential...". Thus, a critical aspect of a mutagen risk assessment (MRA) of drug substance or drug product degradation is the determination of degradation pathways and associated degradation products that are relevant to the manufacturing processes and/or proposed packaging and storage conditions." As discussed above, stress testing is the experimental tool that provides the foundations (e.g., understanding potential degradation pathways and developing sound stability-indicating analytical methods) for such determinations.

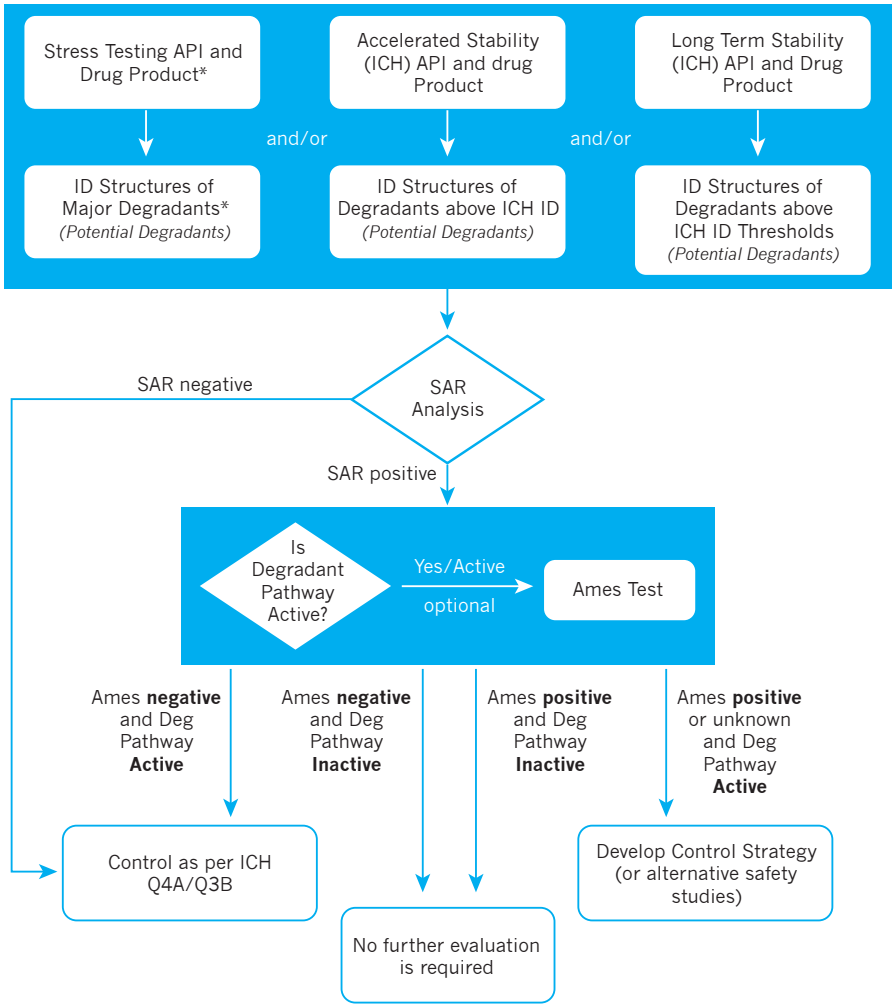


Figure 6. Proposed process flow for assessing degradants in drug substances and products. Reproduced from ref. 47.

Another challenge associated with these mutagenicity predictions of potential and actual degradation products is databasing of the results of the predictions along with the rationale and interpretation of the predictions in the context of specific impurities/degradation products. The retrievability of such information in the context of the metadata can be of great value as the drug moves through development and into the market.

B. Designing and Optimizing Chromatographic Separations and Detection

Chromatographic method development for stability-indicating impurity methods can be greatly simplified using computer software (e.g., ACD/AutoChrom™,[48] DryLab™,[49] and ChromSword™,[50]); such software facilitates the optimization of chromatographic separations of impurities/degradation products. Once partially degraded samples have been generated from a stress testing screen, with just a few laboratory experimental separations, these software packages allow parameters such as pH, temperature, buffer concentration, solvent/modifiers to be chosen and optimized. Examples of such computer-assisted method development have been documented in the literature.[51-56]

C. Elucidating Degradation Product Structures

The elucidation of structures of degradation products is an important aspect of understanding the intrinsic stability of a drug molecule.[57,58] A critical question is whether or not degradation products arising from stress testing studies should be identified. There appear to be two major schools of thought on this issue:[58,59] (1) structure elucidation need only occur for those products formed during formal long-term stability studies above identification thresholds established by ICH Q3A/B, and (2) identification of the major products observed during stress testing. The first approach relies on the quality and rigor of the analytical methodologies and has been called a "technique-oriented" approach,[58,59] because it relies on the analytical technique to provide comprehensive and accurate detection. The second approach involves using stress testing to develop an understanding of potential degradation pathways/chemistry, as implied by the ICH Q1A definition of stress testing. Such an approach has been called a "chemistry-guided" approach.[58,59] The chemistry-guided approach relies on "scientific evaluation of the chemistry to guide the interpretation of the data and the selection of appropriate analytical techniques. An essential part of the chemistry-guided approach is developing an understanding of the structures of the major degradation products observed by the analytical method, which in turn allows an evaluation of the pathways, leading eventually to a rational assessment of the completeness of the investigation and the appropriateness of the analytical methodology."[59] Indeed, it is difficult to understand how stress testing can help develop an understanding of the *intrinsic stability* characteristics of a drug without determining structures of the major degradation products.

Another complication of structure elucidation is the *confidence* in the structure determination. Is the structure simply a "proposed" structure, based on some spectroscopic evidence (typically LC/MS derived), or is it a "confirmed" structure, where the structure is definitive and unambiguous (typically involving full characterization from complete MS and NMR studies and/or chemical synthesis, or partial characterization with a compelling chemistry argument)? Interestingly, Dow *et al.*[60] have proposed that it is important to have confirmed structures (when possible) prior to evaluation for potential mutagenicity per ICH M7; many companies have adopted such an approach.

There are computer tools that have been developed to aid the elucidation of molecular structures based on spectroscopic characterization data.[61,62] Such computer-assisted structure elucidation can be a tremendous tool, aiding human interpretation and helping to avoid "pitfalls caused by mental traps".[61] ACD/Structure Elucidator Suite provides the elucidation scientist with access to vast spectral libraries (including the PubChem database) as well as computational assistance with interpreting NMR, MS, UV/Vis, FT-IR, and *chromatography* data. Dereplication can be especially powerful, using internal and external libraries to search for previously determined structures.

D. The Challenge of Effectively Managing Stress Testing Data

Stress testing and various associated fields (physical property determinations, spectroscopic characterizations, mutagenicity/toxicity testing, method development, stability programs, etc.) present a problem to the drug development process: how can large amounts of data from disparate computer systems, potentially in disparate organizations, acquired over a multi-year timeframe, be organized and leveraged to

enable/speed drug development? Characteristics of a useful product would include:

- Chemical-intelligence
- The ability to import, create, store, track, retrieve and process reports and analytical/spectroscopic data from multiple vendor/instrument formats
- Capabilities for visualization of data in ways meaningful to the scientist and project; visualization and analysis of kinetic timepoints
- The ability to probe multiple LC/UV/MS datasets to search for specific impurities (e.g., theoretical or known degradation products)

As can be inferred, the amount of information described above that can accumulate during the development of a drug can be difficult to organize and can create an "information overload" for those carrying out, organizing, storing, interpreting, and sharing the data/results.

1. Software for Data Management and Decision-Support in CMC

Luminata™,[64] is a product by ACD/Labs designed to address this potential "information overload" problem, not only for stress testing and the associated disciplines, but also for chemical process development, formulation development, impurity investigations and associated control strategies, to name a few. Luminata enables the systematic capture, review, query, visualization, storage, and reporting of many types of data to enable the transformation of data into information, and information into knowledge, facilitating collaboration and decision-making. Examples of some of the types of data handled include:

- Process and degradation-related impurities (structures/identifiers)
- Process schemes and degradation pathway schemes
- Interpreted spectra
- Chromatograms, methods, and data
- Kinetics data
- LC/UV/MS data (can import files for most major instrument vendor formats)
- Toxicity and physicochemical data

Synthetic routes for making APIs are generally represented visually in a chemical structure scheme that shows linear or convergent routes, starting with structures of the basic building blocks (starting materials), reagents, abbreviated conditions for each step, synthetic intermediates, by-products, and the final synthesized API structure. Luminata was developed to capture such chemical process schemes with live structures and ties to the data associated with the process (e.g., specific batches, supporting analytical data, reports, etc).

Stress testing is almost the opposite. Instead of being the end product of a synthetic route, the API is the starting material for degradation under various stress conditions. The API is exposed to various conditions, facilitating degradation into various products associated with the specific stress conditions. Luminata allows for the intuitive representation of such degradation schemes (by condition), as shown in Figure 6. Some of the innovative features include color-coding of structures (e.g., to delineate stress conditions and associated degradation products), associated analyses, kinetic plots, spectroscopic characterization data, and interpreted reports.

Another powerful tool is the ability to "handle" theoretical degradation products. Luminata can understand and process SDfiles containing structures of impurities/ degradation products, either created by the user or as an output file from Zeneth, allowing the scientist to visualize the theoretical degradants in the stress testing map as shown in Figure 7 (left panel). Luminata can then use the structures to probe LC/UV/MS datasets (from a wide array of vendor formats[65]) from various stressed samples for the presence of theoretical or known degradation products. This provides scientists an automated way to assess whether known or theoretical degradation products were formed under any specific stress condition, at user-defined thresholds/levels.

The degradation/stability scientist can also use Luminata to easily create kinetic plots, e.g., loss of parent, increases of specific degradation products over time (see lower right-hand panel in Figure 7). Such kinetic plot visualizations are useful for degradation pathway mechanistic investigations.

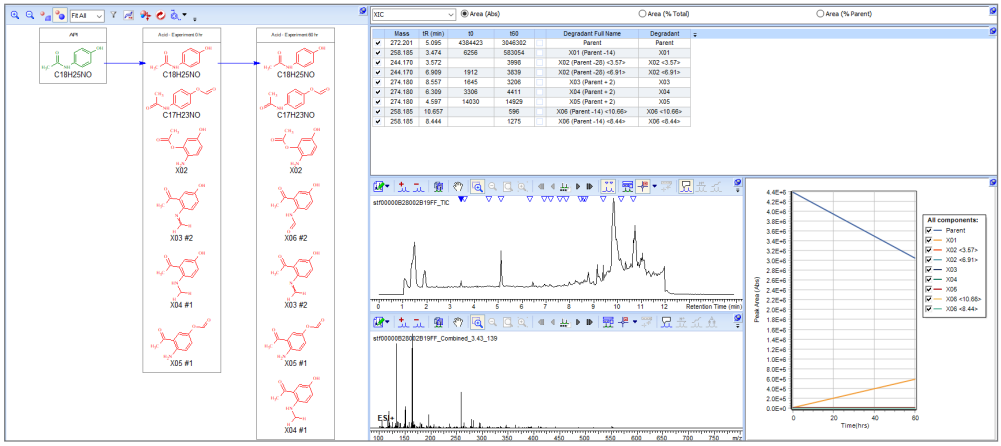


Figure 7. Screenshot of Luminata software, showing how stress degradation processes can be visually represented, with structures associated with conditions and relevant analytical data and reports.

Furthermore, scientists can produce a degradant map with both the theoretical and observed degradants in one location (Figure 8). This information is traditionally stored in several locations, making access to the information difficult.

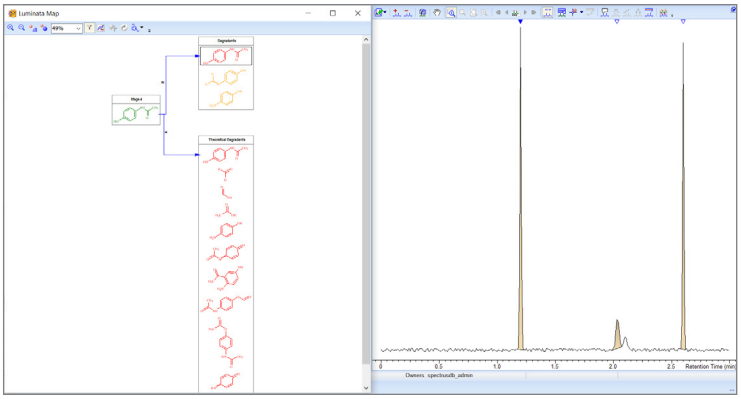


Figure 8. Luminata screenshot showing a degradation map that includes theoretical degradants (lower structure panel, red structures) and degradants detected (upper structure panel, red and yellow structures) in a partially-degraded sample (HPLC chromatogram on right).

III. Prospects for the Future

A. Improvements in Stress Testing Study Tactics

1. Reaching Consensus on Stress Testing Conditions and Endpoints

As described in the introduction, global regulatory guidelines for stress testing are general in nature and vague, with the exception of the detailed legislation/guidelines of ANVISA. It is hoped that harmonization of regulatory expectations will increase as time passes. It will likely take additional scientific investigations and publications in the literature to progress the consensus on the specifics of the most appropriate stress conditions and endpoints.

2. Speeding up Stress Testing through Automation and Informatics Tools

The conditions and endpoints for stress testing are fairly limited and can be achieved in relatively short periods of time. Areas that are poised to provide further gains in resources to conduct such studies include:

- Experimental automation (instrumental automation of weighing, dissolving, diluting, storing at condition, retrieving at specific time points, sample prep/dilution, chromatographic separation)
- Processing automation (integration, quantification, peak tracking, UV-Vis/MS acquisition)
- Interpretation of data (informatics tools)
- Report writing (informatics tools, templates, etc.)
- Ability to calculate or utilize BDE calculations

B. Improvements in Rationalizing Chemical Degradation Pathways

While the development of ab initio and semi-empirical computational approaches[66] hold great promise in the long run for prediction of degradation pathways, the current approaches require a high degree of computational expertise and computing power, making such approaches impractical for many if not most researchers. There are two main tools (in the opinion of the authors) that are currently being developed that will contribute in a significant way to increasing the ability to predict chemical degradation pathways: (1) Zeneth, and (2) the Chemical Transformation Simulator (CTS).[67] Zeneth is actively being developed and improvements over time have been documented.[38]

The CTS is a web-based software tool that will utilize an abiotic (i.e., non-enzymatic) hydrolysis reaction library incorporating chemical moieties known to be susceptible to hydrolytic instability. The reaction schemes are ranked using reported hydrolysis rates to enable qualitative predictions of which site in a molecule is most likely to be hydrolyzed when multiple fragments are present in the molecule of interest. While this tool may be somewhat limited in its planned prediction capabilities, it will provide useful information and the opportunity for extension beyond hydrolysis.

1. Future Development of Informatics Tools

As described above, continuing advancements in analytical and spectroscopic capabilities create an "information overload" problem, which in turn creates an opportunity for innovations in informatics tools. Luminata is one such tool, and future

development already planned for this software includes:

- Sophisticated interfacing with electronic laboratory notebook systems
- Integration with chemical degradation prediction tools (integration with Zeneth has already been accomplished)
- Integration with industry standard physicochemical predictions tools developed in-house for more than 2 decades
- Integration with structure elucidation/spectroscopic interpretation aids
- Integration with chromatographic tools for optimization of selecting a stability indicating methods

IV. Summary

Pharmaceutical stress testing as a field has matured greatly in the last 20 years and will continue to progress as degradation chemistry knowledge grows and associated analytical, spectroscopic, automation, and informatics tools are invented, developed, and implemented. It is hoped that progress in harmonization of conditions and endpoints will continue, as regulatory guidelines become more globally aligned and as the published literature documents the science with successes and failures. As the industry continues to struggle with speeding drug development while reducing costs, the failure rate of new drugs introduced into development is the largest single factor driving the strategy of how thorough stress testing is conducted at early vs. late stage development.

Analytical and automation tools will continue to evolve, speeding experimental set up and analysis, and increasing demands on informatics tools. Such informatics tools will hopefully be positioned to facilitate the transformation of data to information to knowledge and ultimately for the human mind to make good, informed, intelligent judgments and wise decisions. If not, we run the risk of becoming lost in a flood of data and information; such a scenario could result in the scientist longing for the "good old days", when we had less automation, and more time to think about the experiments conducted and interpret the results obtained!

About the Authors

Dr. Steven Baertschi is President of Baertschi Consulting, a firm specializing in solutions to the most difficult stability, impurity, analytical, solid-state, and formulation issues. Retiring from Lilly in 2015, he brings more than 29 years of experience in the pharmaceutical industry to his consulting firm. Dr. Baertschi has organized / Chaired numerous scientific conferences / symposia on stress testing, stability, photostability, and impurities, and has published extensively in these areas, including two editions of a book on pharmaceutical stress testing / drug degradation. Dr. Baertschi is a member of the American Chemical Society (1980), the American Association of Pharmaceutical Scientists (AAPS, 1993), is a Fellow of the AAPS (since 2007).

Joe DiMartino is the Luminata Solution Manager at ACD/Labs. Prior to his current role, he was part of the Technical and Scientific Support Team, where he worked as a Senior Application Scientist.

Previous to his career at ACD/Labs, Joe worked in drug development at Apotex Pharmachem, Inc. His responsibilities included the design of optimized procedures for the synthesis of active pharmaceutical drugs. He was also an integral part of a team that synthesized potential impurities. Joe earned his Bachelor of Science at the University of Winnipeg, and his Graduate Degree in Chemistry at the University of Windsor.

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