

ASAP regulatory strategy: J&J experience

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ONE TEAM Making the Difference for Patients WORLDWIDE



Applications of ASAP

Drug Substance	Drug Product
NME and Salt screening - support for NME selection	Formulation screening
Synthetic routes comparison	Manufacturing process evaluation
Supplier evaluation	Packaging selection
Investigations	Investigations
Specification setting support Retest period/Storage conditions prediction	Specification setting support Shelf life/Storage conditions prediction

Janssen Filing Experience

- **Early Development Clinical Trial Applications (CTA)**
- **Submitted for 5 different projects**
- **Applications:**
 - DS retest
 - DP Shelf Life (Oral Solid Dosage form, Parenteral & Liquids)
 - bridge API synthesis methods
- **Common CTA template: ASAP in 3.2.S.7 and 3.2.P.8**
- **Commitment to perform ICH stability**

Common CTA template: ASAP in 3.2.S.7 and 3.2.P.8

- Introduction to ASAP
- Arrhenius equation (with brief explanation)

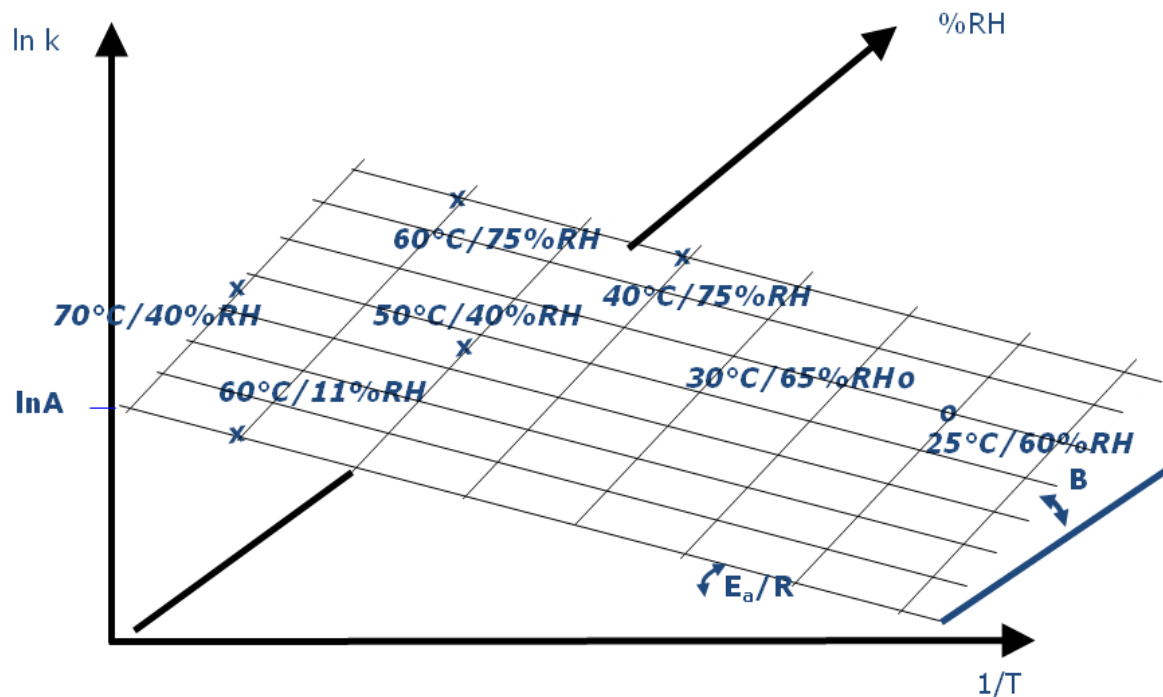
$$\ln k = \ln A - E_a/RT + B(RH) \text{ (Humidity adjusted)}$$

$$\ln k = \ln A - E_a/RT$$

- 3-D/2-D Graph of tested conditions (Generic)
- Stability protocol with general explanation of protocol choice
- Graphical presentation of the formation of the degradation product in function of time
- SL/retest prediction
- Table of data available at tested conditions (as provided for ICH conditions)

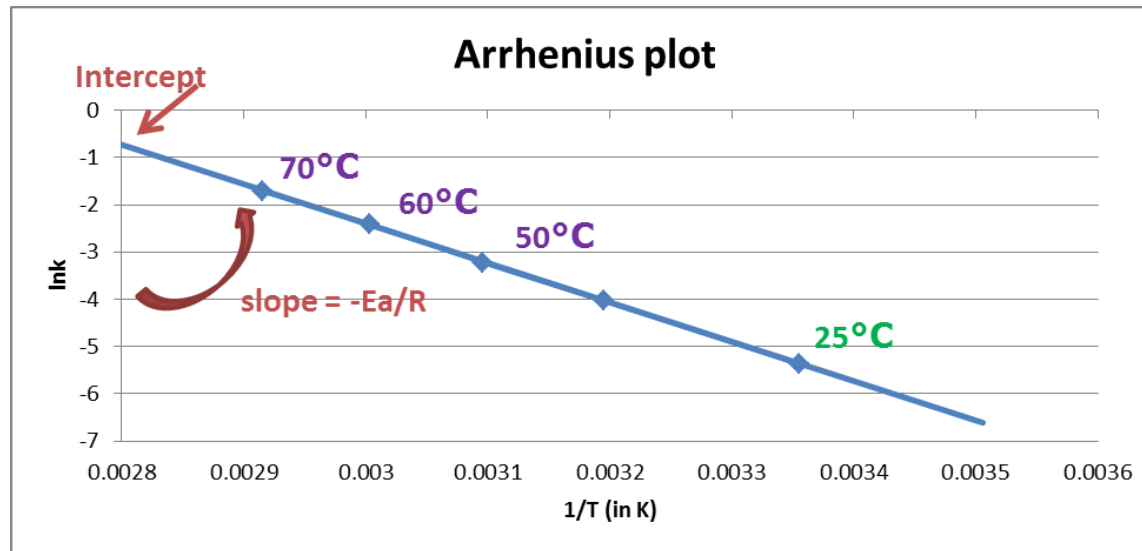
ASAP Presentation in IMPD: solids

- $\ln k = \ln A - E_a/RT + B(\text{RH})$

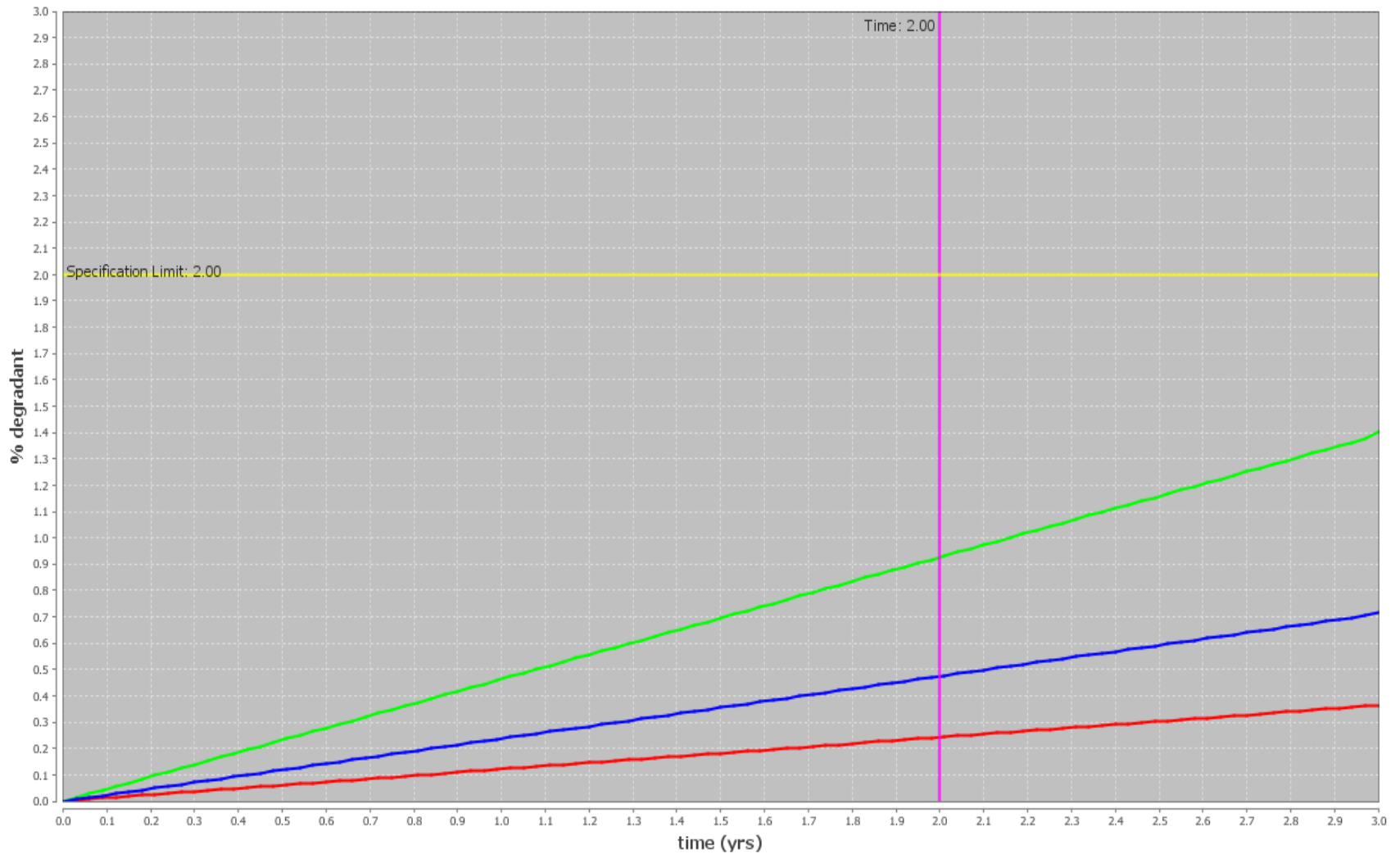


ASAP Presentation in IMPD: liquids

- $\ln k = \ln A - E_a/RT$



Degradation prediction



Feedback HA's

FreeThink Technologies Reported Experience - IND's and generics:

- **Accepted as is:** US, Canada, Bulgaria, France, Hungary, India, Japan, Philippines, Romania, Slovakia, South Africa, Spain, Taiwan, EU/EM
- **Queries/Rejected:** South Korea, Czech Republic, Ukraine, Germany

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Janssen Filing Experience:

- **Submitted to:** Belgium, France, Spain, US, Canada, Austria, Denmark, Finland, Germany, Netherlands, Norway, Poland, Slovakia, South Korea, UK, Czech, Moldova, Bulgaria, Romania, Georgia, Brazil, Italy
 - **Accepted as is:** Spain, France, Belgium, Canada, Austria, Denmark, Finland, Germany, Netherlands, Norway, Poland, Slovakia, South Korea, UK, Moldova, Sweden
 - **Queries/Rejected:** Spain, Czech, France, Italy
 - addl ICH stab was requested
 - SL prediction for products without any degradation observed

ASAP Regulatory Strategy within J&J

- **Uniform approach in setting shelf life**
- **Clear positioning of ASAP in early development stability testing**
- **Consistent build up of knowledge on degradation kinetics of DS/DPs**
- **Strengthen the position of ASAP in filings with higher number of successful submissions (in common effort with other pharma companies)**

Acknowledgements

- Riet Dams, Hana Prockpova
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- Geoff Ridout, Luc Janssens

BACK-UP SLIDES



PHARMACEUTICAL COMPANIES
OF *Johnson & Johnson*

ICH & ASAP stability in Small Molecules

ICH	ASAP
<p>Long-term: 25°C/60%RH, 30°C/75%RH</p> <p>Accelerated conditions: 40°C/75%RH, 50°C</p> <p>Immediate container</p> <p>1-36 months</p>	<p>Broader range of conditions: (40°C to 80°C, 10 to 75%RH)</p> <p>Open dish studies</p> <p>1 month</p>
<p>In development time frame:</p> <ul style="list-style-type: none">• <u>1M and/or 2M stability data available</u>• Little or no degradation after 1M and/or 2M	<p>In development time frame:</p> <ul style="list-style-type: none">• <u>Time To Failure Experiments:</u> under ASAP conditions we define the time required for degradation to give the specification limit - isoconversion
<p>2 or 4 fold extrapolation</p> <p>based on Arrhenius equation, not specific for each DS/DP, general values based on screening of different pharmaceuticals</p>	<p>Shelf life prediction for 6 - 36 months</p> <p>based on a kinetic understanding of the degradation, specific for each DS/DP</p>