

Assessing the Relevance of Solution Phase Stress Testing of Solid Dosage Form Drug Products: a Cross-Industry Benchmarking Study

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Data Supplied by Participating Organizations



organization	number of drug products	degradation products observed during drug substance & drug product stress testing	relevant degradation products observed during drug product stability studies
Company 1	11	38	38
Company 2	11	49	22
Company 3	7	20	10
Company 4	5	34	10
Company 5	4	123	23
Company 6	6	32	7
Company 7	2	4	1
Company 8	2	33	31
Company 9	8	25	23
Company 10	6	29	8
Total	62	387	173

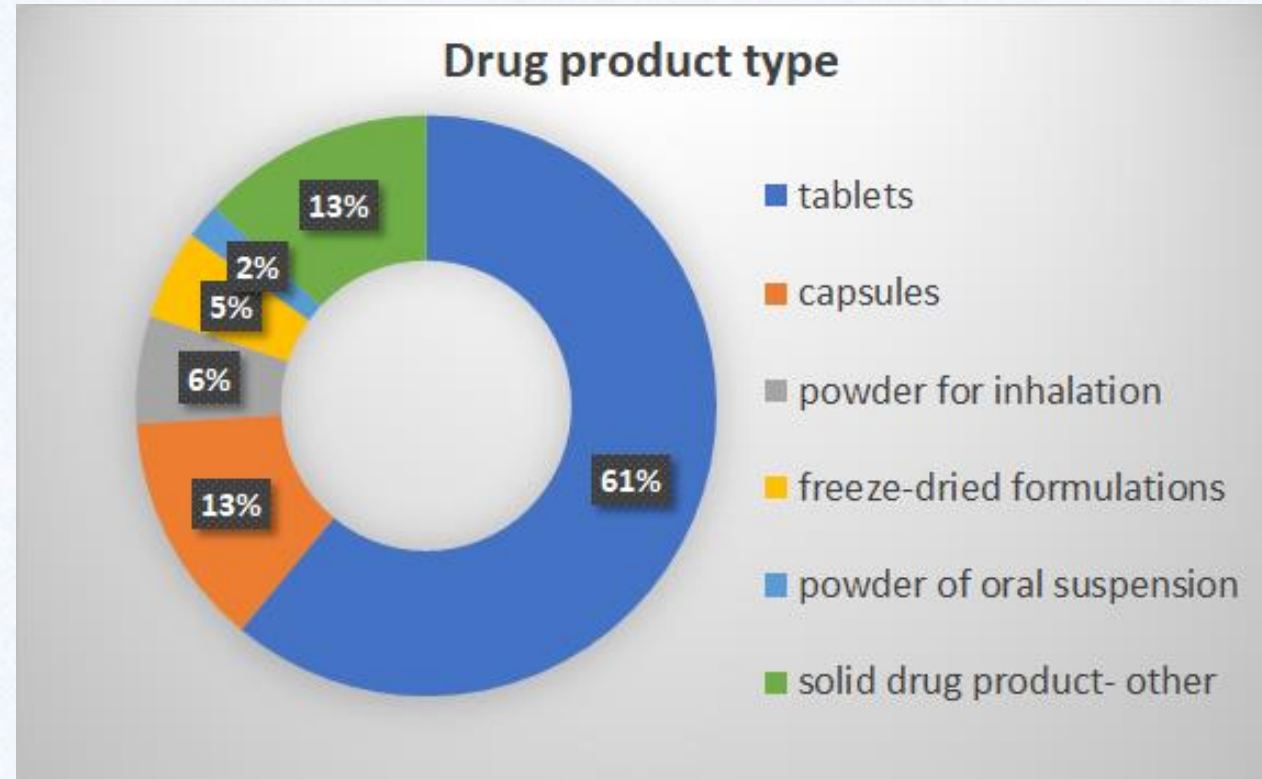
Note: the criteria used for determining which degradation products observed during stress testing should be included in this evaluation varied amongst the participating organizations

Benchmarking data set from 62 drug products

DP that meets the following criteria were prioritized:

- DP has long term stability data available
- Regulatory submissions made or planned
- DP solution stress testing have been performed
- Comprehensive stress testing studies were performed

62 drug products were provided for evaluation



10 combination products included, as well

Comprehensive set of stress condition categories in place for data collection

DS Solution



- Acidic (58)
- Basic (58)
- Peroxide Oxidation (53)
- Radical Oxidation (25)
- Other Oxidation (5)
- Metal ions (43)
- Thermal (17)

DS Solid State



- Thermal (58)
- Thermal/Humidity (49)
- Photolysis (58)

DP Solution



- Acidic Hydrolysis (44)
- Basic Hydrolysis (44)
- Peroxide Oxidation (36)
- Radical Oxidation (20)
- Other Oxidation (2)
- Metal ions (32)
- Thermal (13)

DP Solid State



- Thermal (56)
- Thermal/Humidity (59)
- Photolysis (60)

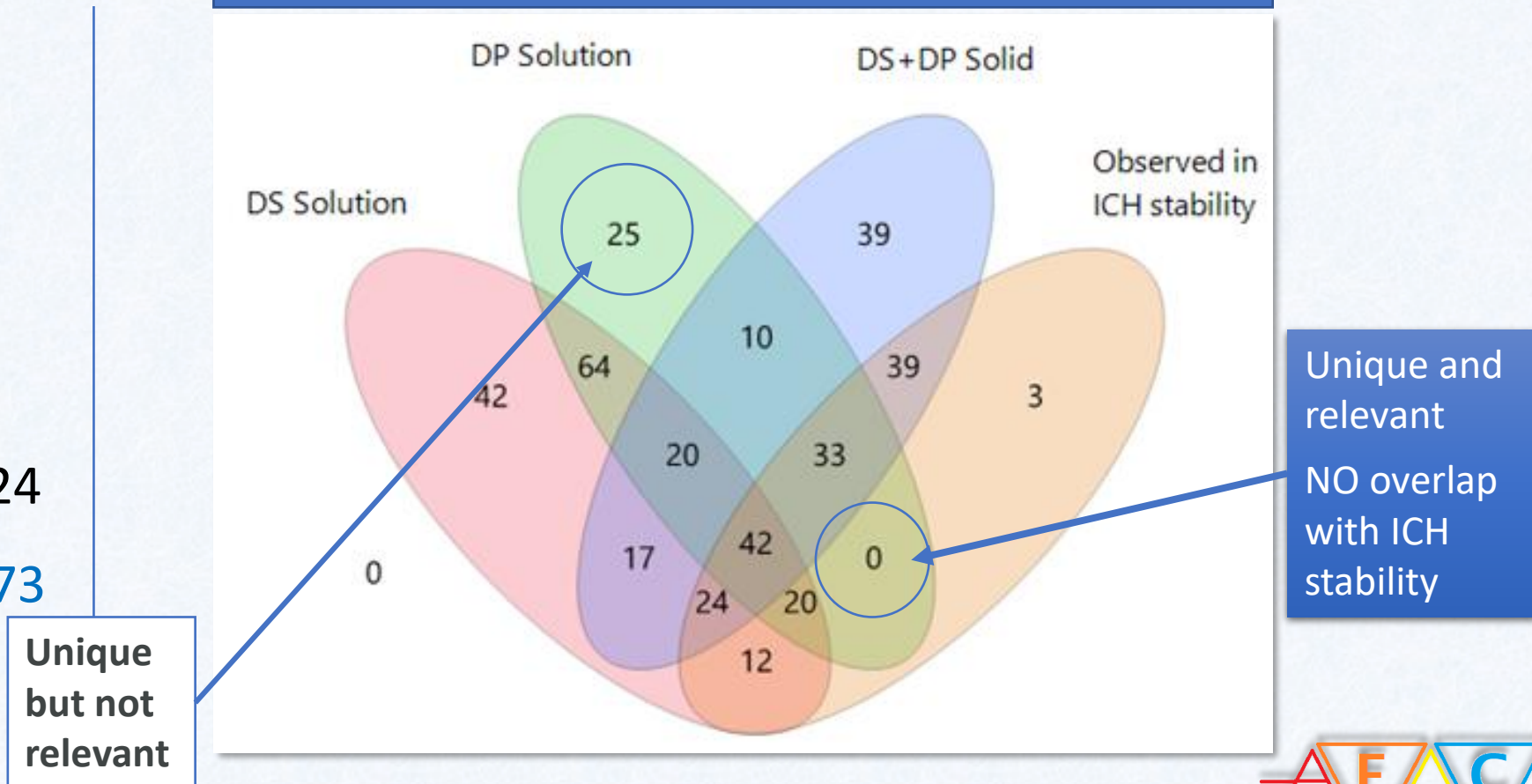
Number in () - number of products subjected to the corresponding stress condition, out of the 62 products in the study

All data received and compiled: Showing distribution of degradation products

Venn diagram shows distribution and overlap of degradation products

- DS solution – 241
- DP solution – 214
- DP & DS solid stability – 224
- **Observed ICH stability – 173**

62 compounds yielded 390 deg products



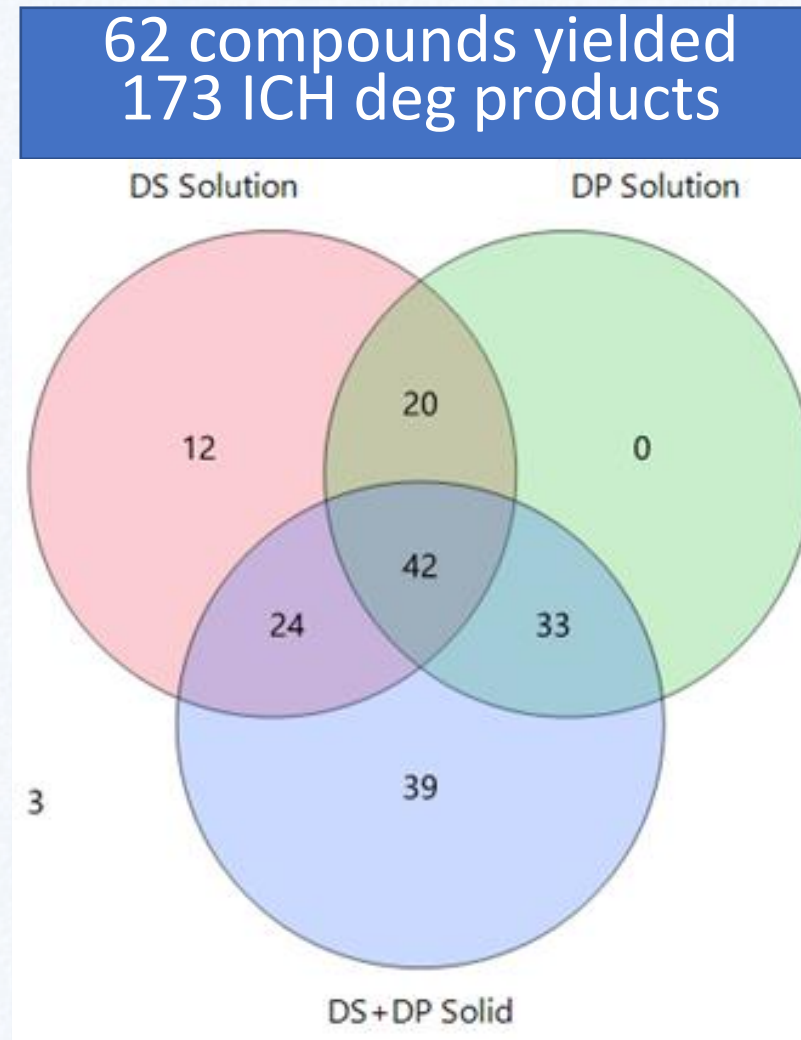
Unique but not relevant

Unique and relevant
NO overlap with ICH stability

Focusing on ICH stability: 173 relevant degradation products

Venn diagram shows distribution and overlap of relevant deg products

- DS solution – 98
- DP solution – 95
 - with NO unique products
- DP & DS solid stability – 138
- Not categorized – 3
 - Appeared in DP in extreme low humidity bottle (i.e., with desiccant)



Solution-phase stress testing of solid drug products

- benchmarking study results

No new unique and relevant degradation products were discovered during solution-based forced degradation of solid dosage products

- 10 organizations offered experimental data from 62 solid dosage products
 - Of these, 387 degradation products were observed
 - Of these, 173 were observed in accelerated or long-term studies and are relevant
 - Of these, 25 of the stress testing degradation products were unique to the solution-phase studies: **but none of these unique products were observed in the formal stability data and are, therefore, not relevant**