Acute Oral Systemic Toxicity Modeling – End User Applications

Lawrence Milchak, Ph.D., DABT
Senior Manager, Toxicology and Strategic Services

April 12, 2018

Since 1902

- Subsidiaries in **71 countries**
- Sales in nearly **200 countries**
- **>90,000** employees
- **200+** factories
- Sales: >**$30B**
- R&D investment: **$~2B**
- **55,000+** products
- **100,000+** patents

Five Business Groups

Industrial

Health Care

Consumer

Safety & Graphics

Electronics & Energy

Toxicology at 3M

Toxicology group resides in the Medical Department

- Corporate staff group reporting through Research and Development

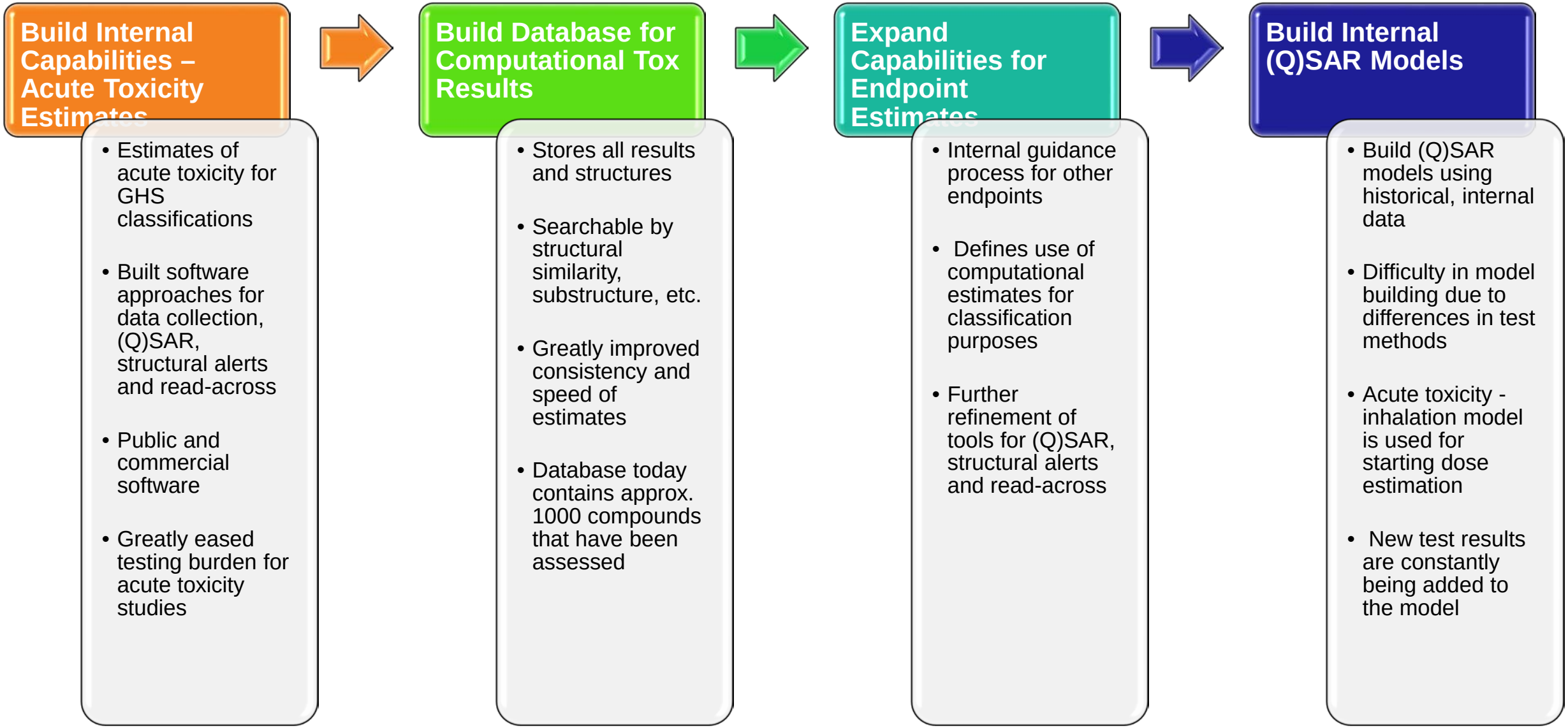
Approximately 25 individuals

- Includes division support toxicologists and the Strategic Toxicology Laboratory (STL)

Centralized resource for toxicology

- Coordinates all global toxicity testing and human health risk assessments

Computational Toxicology Program Development



Acute Oral Systemic Toxicity Estimates

Product development and regulatory applications

- Screening estimates
- Internal hazard profiling
- GHS classifications
- Chemical registrations (REACH, etc.)
- Supporting information for regulatory submittals and risk assessments

Acute Oral Systemic Toxicity Estimates

Approaches	
Combination of (Q)SAR and Read-Across	Applicability domain knowledge is critical
Commercial and Public Software	Most useful on chemistries with low toxicity potential
Multiple tools – weight of evidence approach increases confidence	Add internal data for model building
GHS categories – more confidence in ranges than a single value	Ability to see analogs used to produce the estimate is very useful

Acute Oral Systemic Toxicity Estimates

Successes	Challenges
Weight of evidence approach to increases reliability	Regulatory acceptance for submittals
Minimize reliance on any one tool or approach	Applicability domain issues – no estimates for unique chemistries or unfounded estimates produced
Greatly reduced animal testing on low toxicity chemistries	Limited utility for polymers, inorganic constituents
Experience has helped establish the most useful approaches	Decision making when estimates don’t align

Acute Oral Systemic Toxicity Estimates

Important Considerations for Software

Ease of use and expertise required

Cost and availability – free is best!!

Regulator usage and acceptance

Applicability domain knowledge is critical

Ability to see analogs used to produce the estimate

Ability to add internal historical data for model building

Thank you