



Joanna Edwards – Lhasa Limited

EPAA Conference on Reduction and Refinement –
Combining Excellence in Science and Animal Welfare
Brussels, 30th November 2010

- Established in 1983
- Not-for-profit organisation that promotes knowledge and data sharing in the life sciences
- Controlled by our members
 - Approximately 170 worldwide
 - Pharmaceutical companies
 - Chemical and agrochemical companies
 - Cosmetics companies
 - Universities
 - Contract research organisations
 - Government and regulatory bodies
 - Consultants

 Structure-searchable toxicity database

 Expert system for the prediction of toxicity

 Expert system for predicting metabolic fate

 Expert system for predicting chemical degradation

vitic
NEXUS

derek
NEXUS

meteor

zeneth

- Structure-searchable database offering rapid access to toxicological information
- Contains data on 11,821 substances
- Contains 326,513 data records
- Covers 15 different endpoints
- Contains public, proprietary and regulatory data sources

- Sharing of in-house data between member organisations
- Intermediates
 - Sharing data on the genotoxicity of intermediates
- E-Tox
 - Part of the IMI European project for sharing toxicity data from legacy pre-clinical studies
- Excipients
 - Sharing data on the toxicity of vehicles used in single and repeat dose toxicity studies

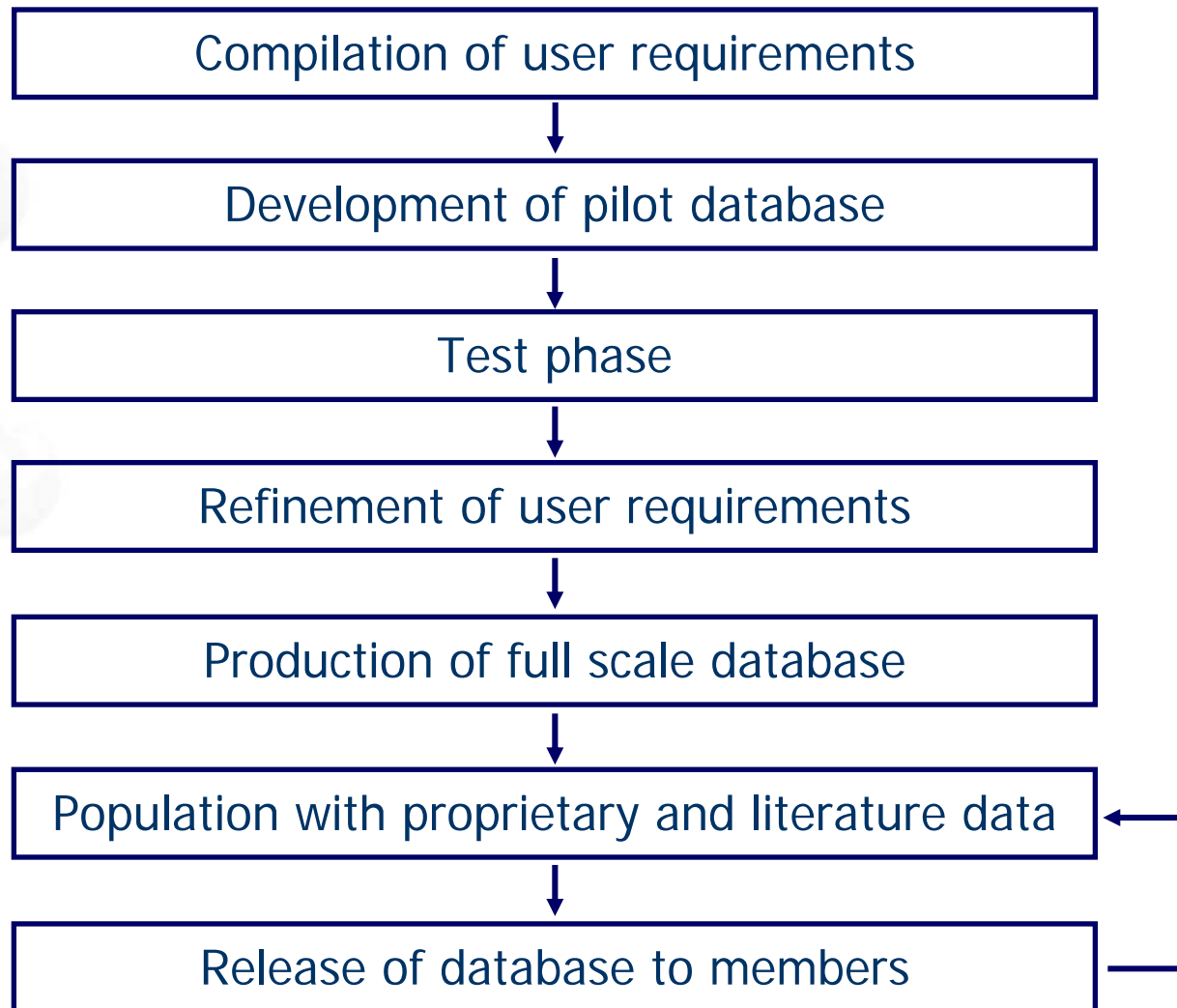
Excipients – An Introduction

- An excipient is any component of a finished drug product other than the active ingredient/s
- Excipients are generally considered to be inactive but they may be associated with toxic effects

Excipients Data Sharing Project - Introduction

- Originated from the Dog Project:
 - Ten pharmaceutical companies plus charities (RSPCA and FRAME) with a shared aim to reduce the amount of animal testing
- A wealth of vehicle toxicity data is held in archives
- Incorporating this into a database would mean less repetition of experiments within companies
- Sharing the data could reduce the number of vehicle control studies carried out by other organisations
- Lhasa Limited approached:
 - to host the database
 - to facilitate data sharing
 - to carry out data entry work

Development Of Excipients Database



Example Questions

- Has a specific vehicle or component been tested in a specific species by a specific route?
- What is the maximum volume and the maximum concentration at which a component has been tolerated?
- Which vehicles have been well tolerated in a certain species? Which were not tolerated?
- Are there studies for combined administration of two specific components?

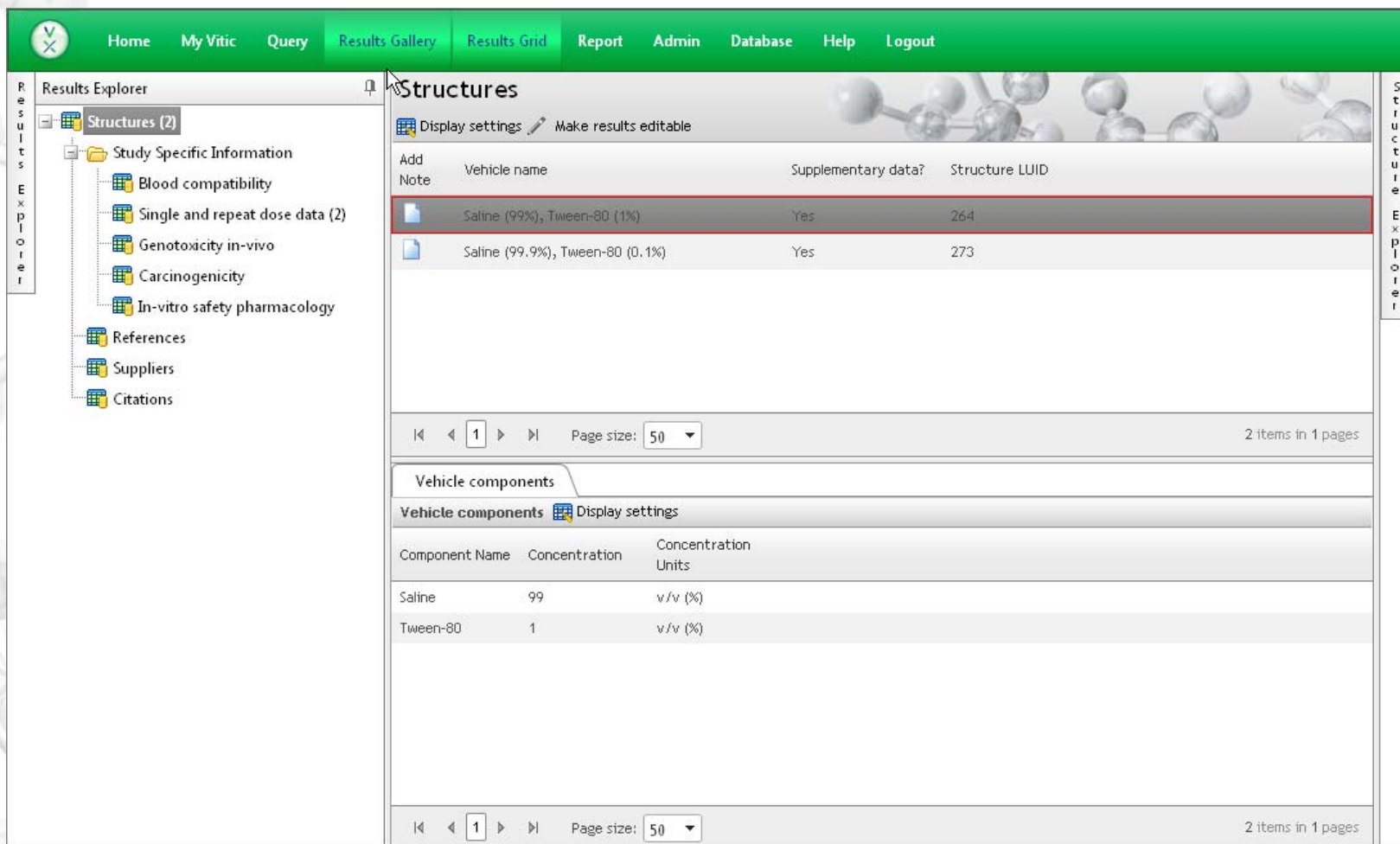
Data priority guidelines

Members donate 50-60 records in the first year with donation in years 2 and 3 being on a quality not quantity basis. Priority is given to vehicles which fit one or more of these guidelines:

- Studies run solely to assess vehicle toxicity
- Unusual/infrequently used vehicles
- Used in long term toxicity studies
- Used in repro/developmental studies
- Any studies with positive findings for vehicle
- Studies that show differences in tolerance with different species or volumes or routes
- Combination vehicles generally more useful than single components

- Single and repeat dose data fields include:
 - Dose volume and dose units
 - Route of administration, frequency and duration of treatment
 - Species, strain, sex and number of animals used
 - Tolerability
- Toxicity inline table data includes:
 - Clinical signs
 - Clinical chemistry
 - Haematology
 - Gross pathology
 - Histopathology
 - Organ weights

Vehicle and component information



The screenshot displays the Lhasa database interface. The top navigation bar includes: Home, My Vitic, Query, Results Gallery, Results Grid, Report, Admin, Database, Help, and Logout. The 'Results Explorer' on the left shows a tree structure under 'Structures (2)' with categories like 'Study Specific Information', 'Blood compatibility', 'Single and repeat dose data (2)', 'Genotoxicity in-vivo', 'Carcinogenicity', 'In-vitro safety pharmacology', 'References', 'Suppliers', and 'Citations'. The main 'Structures' table lists two entries:

Add Note	Vehicle name	Supplementary data?	Structure LUID
	Saline (99%), Tween-80 (1%)	Yes	264
	Saline (99.9%), Tween-80 (0.1%)	Yes	273

Below the table, the 'Vehicle components' section is visible, showing a table with the following data:

Component Name	Concentration	Concentration Units
Saline	99	v/v (%)
Tween-80	1	v/v (%)

Single and repeat dose toxicity information

Home My Vitic Query Results Gallery **Results Grid** Report Admin Database Help Logout

Single and repeat dose data

Display settings Make results editable

Add Note	Vehicle name	Dose volume	Dose units	Treatment duration (VC)	Frequency of admin.	Species	Strain	Tolerability	Approx. age at start of treatment	No. animals per group (both sexes)	Route of admin.	Injection rate (for IV bolus) (ml/min)	pH	Mortality
	Saline (99.9%), Tween-80 (0.1%)	1	ml/kg	1 Days	1/day	Dog	Beagle	Not tolerated	Adult	2	Intravenous (bolus)	6	No info	None
	Saline (99%), Tween-80 (1%)	1	ml/kg	1 Days	1/day	Dog	Beagle	Not tolerated	Adult	1	Intravenous (bolus)	6	No info	None

Page size: 50 2 items in 1 pages

Bone marrow exam Citations - Single and repeat dose data Physicochemical data Reproductive toxicity **Free text - Single and repeat dose data** Urinalysis

Clinical chemistry Clinical signs Electron microscopy Gross pathology Haematology Histopathology Immunotoxicology Organ weights

Clinical signs

Display settings

Clinical signs - Category	Clinical signs - Observation
Breathing	Panting
Skin/fur	Erythema
Locomotive behaviour	Motor activity reduced
Varia	Vomiting
Skin/fur	Scratches

Page size: 50 1 items in 1 pages

2.5 years into initial phase

- 1050 studies donated
- 136 literature records entered
- 454 different vehicle compositions
- 8 different species
- 9 different routes of administration

Feedback and future plans

- ④ 2nd release was in June 2010
- ④ After the next release in March 2011 most members will enter the maintenance phase of the project
- ④ Members have found the database useful in deciding which vehicles to use and in negating the need for additional vehicle control groups
- ④ We are actively promoting the database to attract new members
- ④ Continuation will be decided by current members

Summary

- Consortium of pharmaceutical companies sharing data on vehicles used mainly in single and repeat dose toxicity studies
- Useful in deciding which vehicles to use and in negating the need for additional vehicle control groups
- Reduces the number of animal experiments carried out in organisations

Thank you for your attention