Beyond your data

World-class services for the pharmaceutical industry

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4Pharma

- Established in Turku, Finland in 2002
- Employs ~20 professionals, of which 15 statisticians
- Has offices in Finland (Turku, Espoo), Sweden (Stockholm) and Switzerland (Basel)
- Provides local, professional services for life science companies, primarily in the pharmaceutical industry

Company 4you

- Has exceptional pharmaceutical industry experience
- Excels in statistics, data management, data warehousing, information technology and medical services
- Works today with ~50 customers in Finland, Scandinavia, Central Europe and the US
- **www.4pharma.com**

Services 4you

Services In Statistics

- Study design and sample size calculation
- Statistical programming, analyses and reporting
- Bioinformatics
- Epidemiology
- Tailored training in statistics
- Data visualization
- Statistical consultation

Services in Data Management

- eCRF/CRF design
- Database design
- Data entry
- Data validation and discrepancy management
- Data integration
- Data standardisation (CDISC)
- Consultation at any level

Services 4you

Information Technology expertise

- Interactive Web Response System
- Extranet (documents & information)

Medical services

- Medical writing/coding (MedDRA, WHO-DD, ATC)
- Full clinical study (through partners)

Competence 4you

Global regulatory experience:

- Overall responsibility for Statistics and Data Management
- Electronic submissions
- Face-to-face meetings with FDA, EMA and PMDA
- FDA advisory board meetings
- Participation in FDA site audits

Key role in projects leading to regulatory submissions:

- 1990 or earlier
  - Animal sedatives: DDA
  - Breast cancer: Fareston
  - Parkinson's disease: Comtess/Comtan
- 2000 ->
  - Contraception: Mirena
  - [Sedation: Precedex]
  - [Acutely compensated heart failure: Simdax]
  - Parkinson's disease: Stalevo
  - Glaucoma: Taflotan
- 2010 ->
  - Cryopyrin-Associated Periodic Syndromes (CAPS), Kineret®

Facts 4you

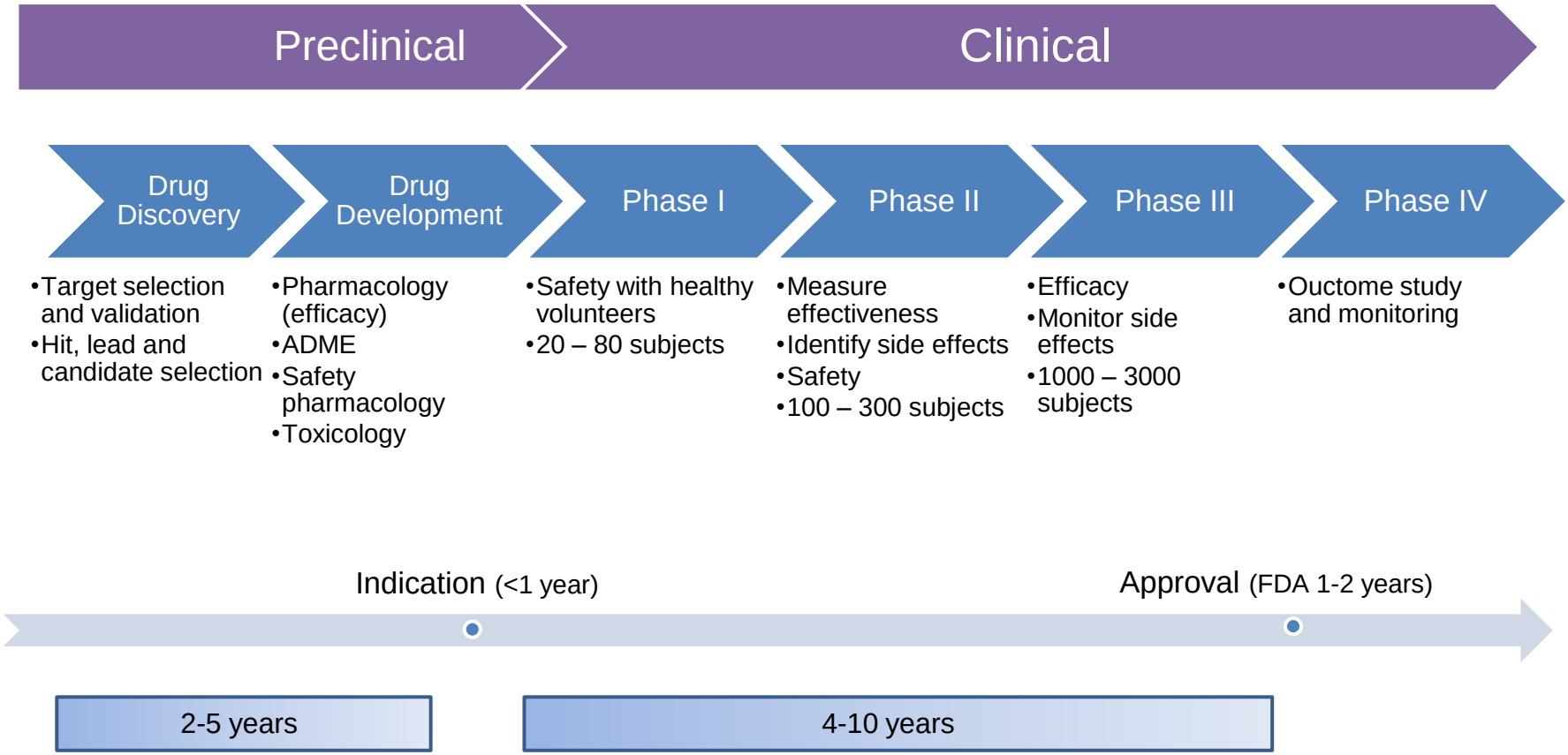
Key role in ongoing projects leading to regulator submissions:

- FDA: 8 projects
- EU: 9 projects

35 studies simultaneously operative:

- Phase I: 7 studies
- Phase II: 3 studies
- Phase III: 10 studies
- Phase IV: 5 studies
- Academic: 4 studies
- Non-pharma: 4 studies
- Other: 2 studies/projects

Clinical trials



SAS and 4Pharma

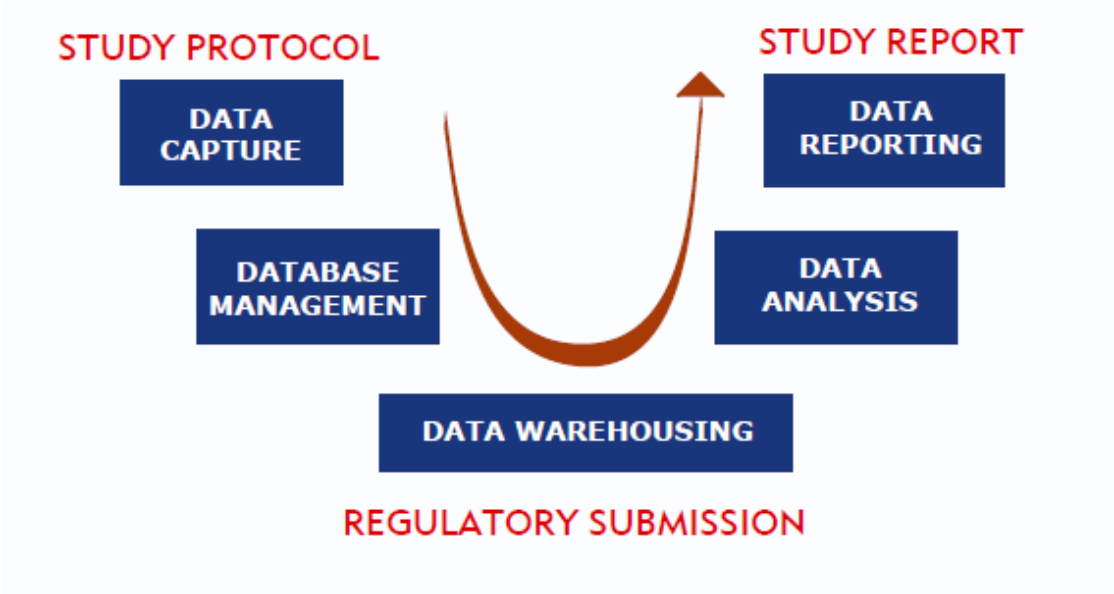
Data Management

- Data standardisation (CDISC)
- Data entry (paper CRFs)
- Validation
- Creating analysis datasets
  - Merging of treatment code

Statistics

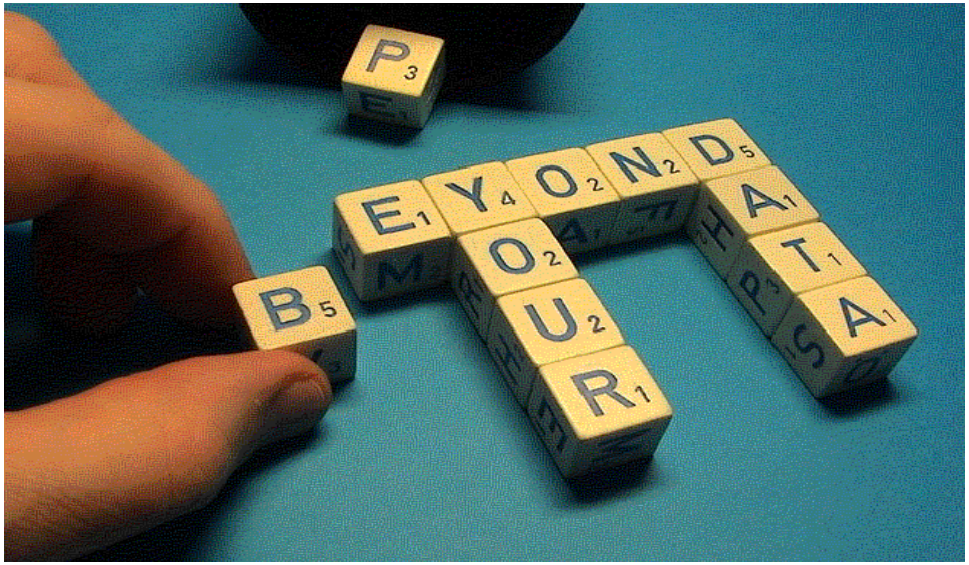
- Sample size calculations and simulations
- Analyses
  - Proc UNIVARIATE, FREQ, MIXED, GENMOD,...
- Tables
  - Proc REPORT
- Figures
  - Proc SGPLOT, GPLOT, SGPANEL,...
- Listings
- Validation

- In many cases MACROs are implented



Validation processes in 4Pharma

- Program validation
- Data validation and verification



Validating user written code

- Three levels of program validation
  - Manual review
  - Manual review + independent calculation of derived variables
  - Completely independent programming
- The study statistician is responsible for deciding the correct type of program validation process for each study
- Validation of data derivation programs
- Validation of programs creating tables, listings, and graphs

Validating user written code

First level program validation

- Manual review of the user written program in order to detect possible errors or discrepancies in the code
- Also includes manual review of the log and output files
  - Log: no errors or warnings can be found in the logs (errorspy-macro)
  - Output: e.g. number of patients and/or events is correct
- Process is repeated until no discrepancies are found

Validating user written code

Second level program validation

- In addition to first level program validation, all derived variables calculated independently and compared against the original values
- Process is done both in the data derivation programs and in programs creating the tables, listings and graphs
- No need to create the final output files
- Process is repeated until no discrepancies are found

Validating user written code

Third level program validation for tables, listings, and graphs

- The Program Validator independently codes the programs for creating all the output files.
- Validation program output files are compared between the original tables, listings and graphs
- If any discrepancies are found, the Program Validator informs the study programmer, who will do the necessary corrections to the programs.
- The Program Validator fills in all the discrepancies and actions taken in correcting these in the Program Validation - document
- Process is repeated until no discrepancies are found

Validating user written code

errorspy - Notepad

File Edit Format View Help

```
WARNING: The variable RESPONSE in the DROP, KEEP, or RENAME list has never been referenced      class.log
ERROR: File SASHELP.CASS DATA does not exist                                                     class.log
WARNING: The data set WORK.CLASS may be incomplete. when this step was stopped
there were 0 observations and 0 variables                                                        class.log
WARNING: Data set WORK.CLASS was not replaced because this step was stopped                      class.log
WARNING: Multiple lengths were specified for the variable CLASS_NAME by input
data set(s). This may cause truncation of data.                                                  examn.log
NOTE: Variable EXAM_DATE is uninitialized                                                        examn.log
```

errorspy - Notepad

File Edit Format View Help

```
Congrats! No errors or warnings were detected!
```

Validating user written code

Third level program validation for datasets

- The Program Validator independently codes the programs for creating the datasets.
- Independent validation process includes comparison between the derived dataset and the dataset created in the validation process.
  - PROC COMPARE
- The Program Validator fills in all the discrepancies and actions taken in correcting these in the Program Validation – document
- Process is repeated until no discrepancies are found

Data validation and verification

Data validation and verification process

- Computerised or manual checks performed on a database to check for:
  - Missing
  - Inconsistent
  - Illogical study data
- Discrepancies can be on the CRF or between the CRF and the database
- The Data Validation Plan (DVP) will be made for each study

Data validation and verification

- Sas programs will be used to perform computerised edit checks
- Edit checks are tested using dummy data, that includes correct, erroneous and missing data for each tested variable
- Edit checks should be executed as a batch run before database lock

Data validation and verification

CHKNO	QUERY	PATID	DATASET	COM1	STATUS
5	Informed consent date is before the date of admission. Please correct.	xxx	dm/ho	Informed Consent:01JAN1900 Date of admission:.	Query
5	Informed consent date is before the date of admission. Please correct.	xxx	dm/ho	Informed Consent:01JAN1900 Date of admission:.	Query
7	Date of birth is missing. Please provide date. / Date of birth is inaccurate. Please correct it.	xxx	dm	DOB:.	Query
8	Date of birth is after the admission date. Please correct it.	xxx	dm/ho	Date of birth:01JAN1900 Date of admission:.	Query
8	Date of birth is after the admission date. Please correct it.	xxx	dm/ho	Date of birth:01JAN1900 Date of admission:.	Query
9	Gender is missing or inaccurate. Please provide data.	xxx	dm	Gender:.	Query
10	Inclusion criteria I02 is not met. Please verify response and provide explanation if correct.	xxx	ie	Criteria:I02 Criteria answer:No	Query
10	Inclusion criteria I03 is not met. Please verify response and provide explanation if correct.	xxx	ie	Criteria:I03 Criteria answer:No	Query
10	Response to inclusion criteria I01 is missing. Please provide data.	xxx	ie	Criteria:I01 Criteria answer:.	Query
10	Response to inclusion criteria I02 is missing. Please provide data.	xxx	ie	Criteria:I02 Criteria answer:.	Query
10	Inclusion criteria I03 is not met. Please verify response and provide explanation if correct.	xxx	ie	Criteria:I03 Criteria answer:No	Query
10	Inclusion criteria I03 is not met. Please verify response and provide explanation if correct.	xxx	ie	Criteria:I03 Criteria answer:No	Query
22	Response to sample collection is missing or inaccurate. Please provide data.	xxx	sp	Sample collected:.	Query
22	Response to sample collection is missing or inaccurate. Please provide data.	xxx	sp	Sample collected:.	Query
22	Response to sample collection is missing or inaccurate. Please provide data.	xxx	sp	Sample collected:.	Query

Thank You