



Public-Source Meta-database Offerings

Supporting Strategic Decision-Making in Clinical Drug Development

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Pharsight
A Certara™ Company

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Introduction: Why Public Source Data Modeling?

The development of a new drug is a high risk and costly activity that involves multiple decisions and tradeoffs

Model-based approaches for combining proprietary data on a specific compound with literature data of likely competitors offer powerful tools for managing:

- Risks concerning dose selection
- Efficient and effective trial design
- Key "go/no-go" decisions

FDA has a growing base of experience with literature modeling and model-based drug development, as part of its Critical Path Initiative

Pharsight Meta-database Offering

Pharsight compiles therapeutic area data and information from public source scientific literature to provide a ready context for model-based meta-analysis that can accelerate quantitative assessment of a compound's performance relative to competing treatments

Pharsight has compiled indication-focused databases in multiple therapeutic areas with a deliberate focus on providing a framework upon which to build decision enabling models

All data are formatted and entered in a “ready-to-model” meta-database that undergoes multiple quality design and check stages

The Pharsight Meta-database Group

Dedicated team functioning within Pharsight Consulting Services (PCS) Group

Provides a quality-driven means of building deliverable public source bibliographies and clinical databases while ensuring that M&S consultants can focus on M&S methods and results

The Meta-database group works collaboratively with PCS therapeutic domain experts and modelers

Responsible for design, assembly, quality control, and maintenance of Pharsight meta-databases

Operates according to proprietary internal procedures

Uses industry-standard tools (e.g., Thomson/ISI[®] Reference Manager[®], Golden Digger[®] software to capture graphical data from industry journals)

Public Data Sources

Public data sources on competitors and analogues from the clinical and scientific literature, collectively called “meta-data”, are diverse and include:

- Published journal articles
- Regulatory documents (e.g., FDA Summary Basis for Approval, EMEA marketing authorization)
- Package inserts or promotional materials from the drug manufacturer
- Published abstracts or poster presentations
- Meeting proceedings
- Web documents (e.g., press releases about new clinical trial results)
- Online clinical trial registries

Utilization of Pharsight Meta-databases

Assess literature and engage clinical teams to address key program questions about NCE attributes vs. competitors

Build dose-response models of the competitive landscape for a new drug before NCE patient-level data are available

Combine public-source literature models with proprietary sponsor/NCE data to produce an evolving picture of a compound's competitive product profile

Update models as new proprietary and public information on the NCE becomes available to assess likely clinical benefits and trade-offs

Make modeling results readily available to the team and communicate predictive results of modeled product profiles using visualization software tools, such as Pharsight's [Drug Model Explorer](#)[®] (DMX[®])

Benefits of Integrated, Comparative Literature Modeling

Make explicit quantitative assessments between competing treatments when no direct within-study comparisons are available

Predict clinical outcomes for NCEs even when no new clinical data are collected

- At unstudied doses
- Extrapolation of steady-state effect from early short-duration dose ranging trials

Bridge preclinical-to-clinical or biomarker-to-clinical relationships within a common therapeutic class

Greater objectivity when predicting and inferring an NCE's critical efficacy/safety/tolerability attributes

- Compare NCE attributes and uncertainty with competing therapies
- Compare with draft launch label targets

Currently Available Public-Source Meta-databases: Summary by Therapeutic Area and Disease/Indication

Therapeutic Area	Disease State/Indications
Anti-infectives	Fluoroquinolone Anti-infectives Hepatitis C Virus (HCV)
Anti-inflammatory	Rheumatoid Arthritis (RA)
Cardiovascular	Congestive Heart Failure (CHF) Hypertension Hyperlipidemia/Dyslipidemia Hypercholesterolemia Thrombosis
Central Nervous System	Depression Migraine Headache Schizophrenia Sleep Disorders (including Excessive Daytime Sleepiness) Alzheimer's Disease
Endocrine	Type II Diabetes Obesity
Gastro-intestinal	Gastro-esophageal reflux disease (GERD) Irritable Bowel Disease (IBD) Chronic Idiopathic Constipation
Genito-urinary	Female Sexual Arousal Disorder (FSAD) Urinary incontinence Benign Prostatic Hyperplasia (BPH)
Pain	Osteoarthritis Pain Chronic Pain
Respiratory	Asthma Chronic Obstructive Pulmonary Disease (COPD)

Anti-infectives Public Source Meta-database: Fluoroquinolones

Time Period: 1993-2006

Clinical Studies Included: 9

References Included: 21

Number of subjects included: >300

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Moxifloxacin, Levofloxacin, Ciprofloxacin, Ofloxacin, Gemifloxacin, Garenoxacin, Gatifloxacin, Sitafloxacin

Scope of Therapies

- Treatment of bacterial infections of various body sites, structures, and severities

Disease State/Indication

- Bacterial infections

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Anti-infectives Public Source Meta-database: Hepatitis C Virus (HCV)

Time Period: 1998-2005

Clinical Studies Included: 3

References Included: 17

Number of subjects included: >300

Literature Sources

- PubMed, Medline

Drugs Included

- Interferon, Interferon alpha, Interferon beta, Pegylated Interferon alpha

Scope of Therapies

- Treatment, induction of remission, and maintenance of remission of Hepatitis C-type viral infection

Disease State/Indication

- Viral infection

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Anti-inflammatory Public Source Meta-database: Rheumatoid Arthritis (RA)

Time Period: 1996-1Q2010

Clinical Studies Included: 44

Named trials included: ARMADA, ASPIRE, ASSURE, ATTAIN, CHANGE, DANCER, MIRROR, RADIATE, REFLEX, STAR, SUNRISE, TEMPO

References Included: 90

Number of subjects included: >34,000

Literature Sources

- PubMed, Medline, Meeting Abstracts, FDA Summary Basis of Approval (SBA)

Drugs Included

- Abatacept, Adalimumab, Anakinra, Certolizumab, Etanercept, Golimumab, Infliximab, Leflunomide, Methotrexate, Rituximab, Tocilizumab

Scope of Therapies

- Drugs intended to mitigate the signs and symptoms of rheumatoid arthritis

Disease State/Indication

- Rheumatoid arthritis

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Cardiovascular Public Source Meta-database: Lipids

Time Period: 2000-1H2007

Clinical Studies Included: 43

Name trials included: ASTEROID, STELLAR, PRINCE, SAFARI

References Included: 74

Number of subjects included: >1,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Atorvastatin, Ezetimibe, Lovastatin, Pravastatin, Rosuvastatin, Simvastatin, Omega-3 fatty acids, Fenofibrates, Ezetimibe/Simvastatin (fixed combination)

Scope of Therapies

- Drugs to treat lipid profile abnormalities

Disease State/Indication

- Hyperlipidemia

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Cardiovascular Public Source Meta-database: Plant Stanols

Time Period: 1994-2005

Clinical Studies Included: 5

References Included: 18

Number of subjects included: >1,100

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Atorvastatin, Simvastatin, Pravastatin, Lovastatin, Ezetimibe, Plant Stanols

Scope of Therapies

- Reduction of low-density lipoprotein (LDL) cholesterol

Disease State/Indication

- Hypercholesterolemia

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Cardiovascular Public Source Meta-database: Bleeding Cascade Disorders and Control (Factor Xa)

Time Period: 1980- 2Q2010

Clinical Studies Included: 62

Name trials included: APPRAISE, ATLAS, BISTRO, ESTEEM, EXPERT, METHRO, PLATO, PETRO
RECORD, RE-MODEL, RE-NOVATE, SPORTIFF, STEEPLE, TRITON, OASIS

References Included: 162

Number of subjects included: >60,000

Literature Sources

- PubMed, Medline, ISI Web of Science, Cinahl, OVI

Drugs Included

- Apixaban, Dabigatran, Dalteparin, Edoxaban, Enoxaparin, Fondaparinux, Heparin, Melagatran, Razaxaban, Rivaroxaban, Tinzaparin, Warfarin, Ximelagatran, Naproxen

Scope of Therapies

- Drugs intended to prevent abnormal or undesired blood clots

Disease State/Indication

- Pulmonary embolism, deep-venous thrombosis, venous thromboembolism, prevention of post-surgical clot

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Cardiovascular Public Source Meta-database: Combination Aldosterone Antagonist/Diuretic

Time Period: 1985-2004

Clinical Studies Included: 1

References Included: 11

Literature Sources

- PubMed, Medline

Drugs Included

- Torsemide

Scope of Therapies

- Treatment of hypertension, congestive heart failure, abnormal fluid pooling or swelling, edema

Disease State/Indication

- Hypertension, edema, congestive heart failure

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

CNS Public Source Meta-database: Antidepressants

Time Period: 1980-2006

Clinical Studies Included: 18

References Included: 129

Number of subjects included: >15,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA), clinicalstudyresults.org

Drugs Included

- Bupropion, Citalopram, Duloxetine, Fluoxetine, Fluvoxamine, Nefazodone, Paroxetine, Reboxetine, Sertraline, Venlafaxine

Scope of Therapies

- Drugs intended to treat clinical and behavioral manifestations of depression

Disease State/Indication

- Major depressive disorder (MDD), mild to severe depression

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

CNS Public Source Meta-database: Antipsychotics

Time Period: 1980-2005

Clinical Studies Included: 11

References Included: 90

Number of subjects included: >7,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Aripiprazole, Chlorpromazine, Clozaril, Haloperidol, Olanzapine, Risperidone, Ziprasidone, Quetiapine, Amisulpride

Scope of Therapies

- Drugs intended to treat clinical and behavioral manifestations of schizophrenia

Disease State/Indication

- Acute and chronic schizophrenia, schizoaffective disorder, schizophreniform disorder

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

CNS Public Source Meta-database: Sleep Disorders

Time Period: 1986-2004

Clinical Studies Included: 3

References Included: 51

Number of subjects included: >3,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Diazepam, Flunitrazepam, Flurazepam, Lorazepam, Lormetazepam, Triazolam, Zaleplon, Zolpidem

Scope of Therapies

- Drugs intended to promote the onset of sleep, to decrease sleep latency, and to treat insomnia

Disease State/Indication

- Primary insomnia, transient insomnia, chronic insomnia

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

CNS Public Source Meta-database: Excessive Daytime Sleepiness

Time Period: 1994-2007

Clinical Studies Included: 5

References Included: 22

Number of subjects included: >1,900

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Armodafinil, Modafinil

Scope of Therapies

- Drugs intended to treat narcolepsy, shift worker disorder, excessive daytime sleepiness

Disease State/Indication

- Improvement of excess daytime sleepiness

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

CNS Public Source Meta-database: Migraine Headache

Time Period: 2000-2006

Clinical Studies Included: 3

References Included: 14

Number of subjects included: >6,000

Literature Sources

- PubMed, Medline

Drugs Included

- Almotriptan, Eletriptan, Frovatriptan, Rizatriptan, Sumatriptan, Topiramate, Zolmitriptan

Scope of Therapies

- Treatment and prophylaxis of signs and symptoms of migraine, cluster, central, and vascular headaches

Disease State/Indication

- Migraine headache treatment and prophylaxis

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

CNS Public Source Meta-database: Alzheimer's Disease

Time period: 1987-1Q2009

Clinical Studies Included: 19

References Included: 66

Number of subjects included: >8,000

Literature sources:

- PubMed, Medline, FDA Summary Basis of Approval (SBA), clinicaltrials.gov

Drugs Included:

- Donepezil, Tarenflurbil, Placebo, Vitamin E

Scope of therapy:

- Treatment of signs and symptoms of Alzheimer's disease

Disease State/Indication:

- Alzheimer's disease

Displays and Summaries:

- Study characteristics, data listings including all extracted data elements
treatment characteristics, database conventions

Endocrine Public Source Meta-database: Diabetes

Time Period: 1988-1Q2010

Clinical studies included: 78

References Included: 175

Number of subjects included: >27,000

Literature Sources

- PubMed, Medline, European Medicines Agency (EMA), FDA Summary Basis of Approval (SBA)

Drugs Included

- Alogliptin, Glimepiride, Glipizide, Glyburide, Exenatide, Liraglutide, Metformin, Pioglitazone, Troglitazone, Rosiglitazone, Saxagliptin, Sitagliptin, Vildagliptin

Scope of Therapies

- Drugs intended to normalize blood sugar abnormalities in the treatment of Type II Diabetes Mellitus

Disease State/Indication

- Type II diabetes mellitus (insulin-dependant and non-insulin-dependant)

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Endocrine Public Source Meta-database: Obesity

Time Period: 1972-2007

Clinical Studies Included: 12

Named trials included: RIO-Diabetes, RIO-Europe, RIO-Lipids

References Included: 74

Number of patients: >30,000

Literature Sources

- PubMed, Medline, Meeting Abstracts

Drugs Included

- Fenfluramine, Orlistat, Phentermine, Rimonabant, Sibutramine, Topiramate

Scope of Therapies

- Drugs intended to promote weight loss

Disease State/Indication

- Obesity, overweight

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Gastro-intestinal Public Source Meta-database: Gastro-esophageal reflux disease (GERD)

Time Period: 1975-2005

Clinical Studies Included: 8

References Included: 70

Number of subjects of included: >18,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA), clinicalstudyresults.org

Drugs Included

- Cisapride, Esomeprazole, Lansoprazole, Metoclopramide, Mosapride, Omeprazole, Pantoprazole, Rabeprazole, Tegaserod, Zaccopride

Scope of Therapies

- Drugs intended for esophageal healing and for control of symptoms

Disease State/Indication

- Gastroesophageal reflux disease (GERD), heartburn, reflux, erosive esophagitis, endoscopy-negative reflux disease, endoscopy-positive reflux disease

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Gastro-intestinal Public Source Meta-database: Irritable Bowel Disease (IBD)

Time Period: 1992-2009

Clinical Studies Included: 30

Named trials included: ACCENT, ACT, CLASSIC CHARM, ENCORE, ENACT, HARMONY, GAIN, GETAID, OLE, PRECISE

References Included: 60

Number of subjects included: >7,000

Literature Sources

- PubMed, Medline, Cinahl, Biosis, European Medicines Agency (EMA), Web of Science, Healthstar, clinicaltrialsresults.org

Drugs Included

- Adalimumab, Alicaforsen, Basiliximab, Certolizumab, Daclizumab, Etanercept, Fontolizumab, Infliximab, Interferon, Natalizumab, Onercept, PEG-IFN, Ustekinumab, Vedolizumab, Visilixumab, Rosiglitazone

Scope of Therapies

- Treatment of signs and symptoms, induction of response and remission, and maintenance of response and remission of Ulcerative Colitis, Crohn's Disease, and Irritable Bowel Syndrome

Disease State/Indication

- Ulcerative colitis; Crohn's disease

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Gastro-intestinal Public Source Meta-database: Chronic Idiopathic Constipation

Time Period: 1998-2007

Clinical Studies Included: 14

References Included: 58

Number of subjects included: >13,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA), clinicaltrials.gov

Drugs Included

- Tegaserod, Lubiprostone, Lactulose, PEG-3350

Scope of Therapies

- Treatment of signs and symptoms of chronic constipation

Disease State/Indication

- Chronic Idiopathic Constipation

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Genito-urinary Public Source Meta-database: Female Sexual Arousal Disorder (FSAD)

Time Period: 2000-2006

Clinical Studies Included: 3

References Included: 25

Number of subjects included: >3,200

Literature Sources

- PubMed, Medline, Cinahl, Biosis, Web of Science, Healthstar, clinicaltrialresults.org

Drugs Included

- Alprostadil, Bremelanotide, Sildenafil, Testosterone, Tibolone, Apomorphine, Bupropion, Esterified Estrogens, Methyltestosterone

Scope of Therapies

- Treatment of sexual dysfunction, lack of sexual interest, and sexual desire disorders in females

Disease State/Indication

- Female sexual arousal disorder; hypoactive sexual desire disorder in females

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Genito-urinary Public Source Meta-database: Urinary incontinence (UI)

Time Period: 1998-2007

Clinical Studies Included: 11

Named trials included: IMPACT, STAR, OPERA

References Included: 32

Number of subjects included: >14,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA), clinicaltrials.gov

Drugs Included

- Tolterodine

Scope of Therapies

- Treatment of signs and symptoms of urinary incontinence

Disease State/Indication

- Treatment of urinary incontinence

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Genito-urinary Public Source Meta-database: Benign Prostatic Hyperplasia (BPH)

Time Period: 1996 2Q2008

Clinical Studies Included: 18

Named Trials: PLESS, PREDICT, PROSPECT, PROWESS

References included: 26

Number of subjects included: >32,000

Literature Sources

- PubMed, Medline, clinicaltrials.gov

Drugs included

- Doxazosin, Dutasteride, Finasteride, Tamsulosin, Terazosin

Scope of Therapies

- Treatment of signs and symptoms of benign prostatic hyperplasia

Disease State Indication

- Treatment of benign hyperplasia

Disease and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Pain Public Source Meta-database: Osteoarthritis (OA) Pain

Time Period: 1989-3Q2007

Clinical Studies Included: 9

References Included: 46

Number of subjects included: >9,000

Literature Sources

- PubMed, Medline, Cinahl, Biosis, Web of Science, Healthstar, clinicaltrialresults.org

Drugs Included

- Oxycodone, Oxymorphone, Codeine, Tramadol, Dextropropoxyphene, Dihydrocodeine, Fentanyl

Scope of Therapies

- Analgesics intended to mitigate painful symptoms of osteoarthritis

Disease State/Indication

- Osteoarthritis

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Pain Public Source Meta-database: Chronic Pain

Time Period: 1989-1Q2010

Clinical Studies Included: 12

References Included: 73

Number of subjects included: >14,000

Literature Sources

- PubMed, Cinahl, ISI Web of Science, Healthstar, FDA Summary Basis of Approval (SBA)

Drugs Included

- Codeine, Dextropropoxyphene, Dihydrocodeine, Fentanyl, Morphine, Oxycodone, Oxymorphone, Tramadol, Tapentadol, Morphine/Naltrexone, Oxycodone/Naloxone

Scope of Therapies

- Analgesics intended to mitigate pain

Disease State/Indication

- Chronic pain

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Respiratory Public Source Meta-database: Asthma

Time Period: 1989-2Q2010

Clinical Studies Included: 20

References Included: 101

Number of subjects included: >48,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Beclomethasone dipropionate, Budesonide, Fluticasone, Formoterol, Indacaterol, Montelukast, Omalizumab, Salmeterol, Theophylline

Scope of Therapies

- Drugs intended to control and treat the symptoms of asthma and to prevent asthma symptoms from occurring

Disease State/Indication

- Bronchial asthma, persistent or chronic asthma, mild to severe asthma

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions

Respiratory Public Source Meta-database: Chronic Obstructive Pulmonary Disease (COPD)

Time Period: 1985-2Q2010

Clinical Studies Included: 72

Named trials included: ECLIPSE, INHANCE, ISOLDE, PEGASUS, RATIO, RECORD, TORCH, TRISTAN, UPLIFT

References Included: 117

Number of subjects included: >60,000

Literature Sources

- PubMed, Medline, FDA Summary Basis of Approval (SBA)

Drugs Included

- Acclidinium, Albuterol, Cilomilast, Fluticasone, Glycopyrronium Bromide (NAV237), Indacaterol, Ipratropium, Roflumilast, Salbumatol, Salmeterol, Tiotropium and Placebo

Combination drugs

- Fluticasone + Salmeterol and Budesonide + Formoterol

Scope of Therapies

- Drugs intended to treat the signs and symptoms of Chronic Obstructive Pulmonary Disease (COPD) and slow the progression of COPD

Disease State/Indication

- Chronic obstructive pulmonary disease

Displays and Summaries

- Study characteristics, data listings including all extracted data elements, treatment characteristics, database conventions