

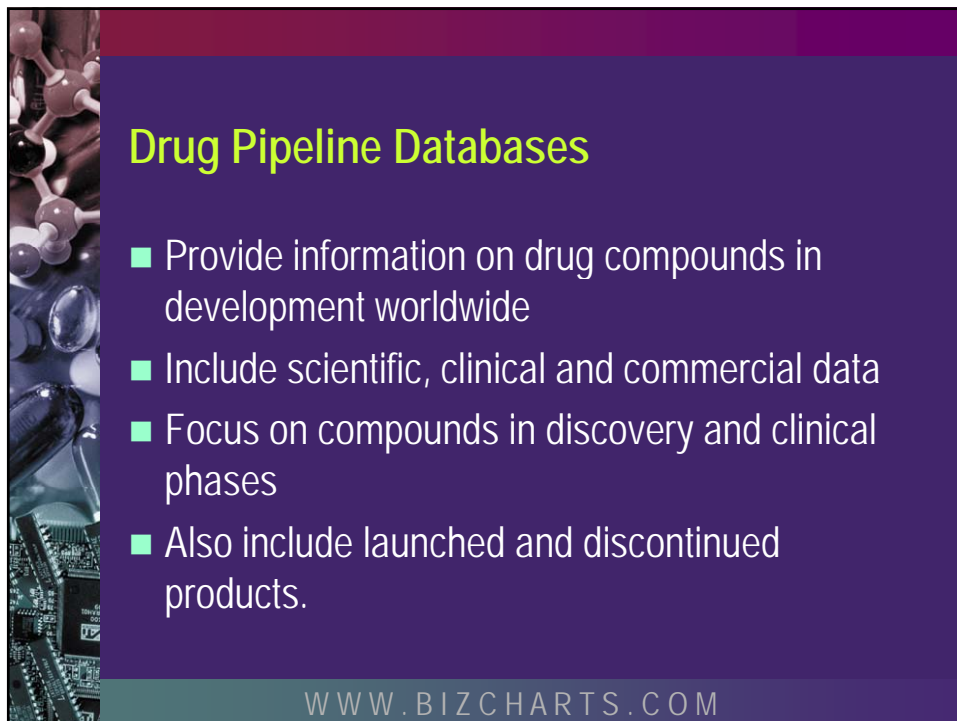
The slide features a vertical strip on the left with images of a molecular model, pills, and a circuit board. The main content area has a white background with a purple header and footer. The BizInt Solutions logo is in the top left, and an illustration of a person surfing is in the top right. The title and subtitle are centered, and the date and website are at the bottom.

BIZINT
SOLUTIONS

Surfing the Pipeline:
Comparing the coverage and content
of drugs-in-development databases

November 2003

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The slide features a vertical strip on the left with images of a molecular model, pills, and a circuit board. The main content area has a dark purple background with a white header and footer. The title is in yellow-green, and the list items are in white. The website is at the bottom.

Drug Pipeline Databases

- Provide information on drug compounds in development worldwide
- Include scientific, clinical and commercial data
- Focus on compounds in discovery and clinical phases
- Also include launched and discontinued products.

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Drug Pipeline Databases -- sample record

FP-21399
 PJB Pharmprojects Accession Number: 22916
 Last Update: 1999-03-23

Originator: Merck KGaA (Germany)

Company Status

Company	Status
Merck KGaA	Phase II Clinical Trial

World Status: Phase II Clinical Trial
Origin of Material: Chemical synthesis, synthetic (CH-SY)

Summary
 FP-21399 is the lead candidate in a series of antiviral organic compounds, under development by Lexigen Pharmaceuticals (Merck KGaA). It does not enter the cell and is therefore thought to be less toxic than reverse transcriptase inhibitors.

Clinical
 It is in Phase II trials (Press release, Merck KGaA, 16 Dec 1998). In a Phase I trial in 34 HIV-infected patients, 9/13 patients on a repeated-dose regimen of FP-21399 1-3mg/kg iv infusion once weekly q 4wks showed an increase in CD4+ cell counts to 15% over their baseline value. It was well tolerated (J Infect Dis, 2000, 182, 607).

Preclinical
 Preclinical studies showed it prevented HIV entry at the cell membrane by interacting with the V3 loop of gp120 on the viral envelope (Scrip, 1995, 2033, 25). Updated by PN on 13/11/2000.

Therapeutic Activity
 Antiviral, anti-HIV (J5A)

Pharmacological Activity
 GP120env antagonist (GP-120-AN)

Therapy Status


Therapy	Pharmacology	Status
J5A	GP-120-AN	Phase II Clinical Trial

Drug Pipeline Databases

The leading players

- **Pharmprojects** -- PJB Publications
- **R&D Focus** -- IMS Health (IMS Global Services)
- **R&D Insight** -- Adis (Wolters Kluwer)
- **IDdb** -- Current Drugs (Thomson)
- plus others: Prous Integrity, F-D-C Reports, Derwent Drug File,...

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Drug Pipeline Databases

Compare the differences in...

- **Coverage** – the number of records retrieved from a particular search.
- **Content** -- the information provided for a compound by each database.

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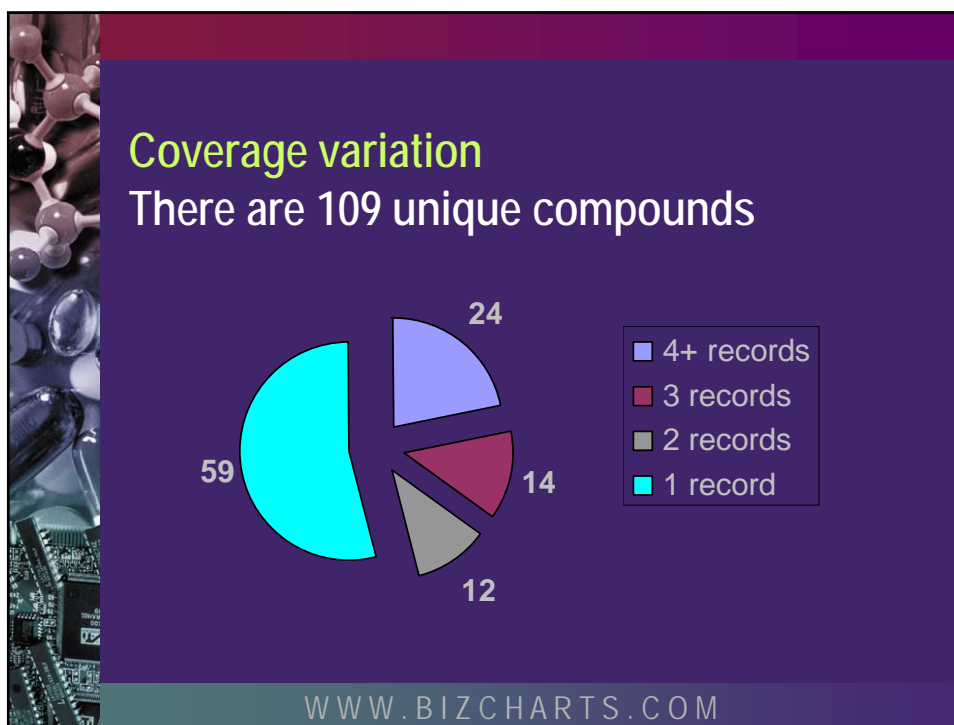
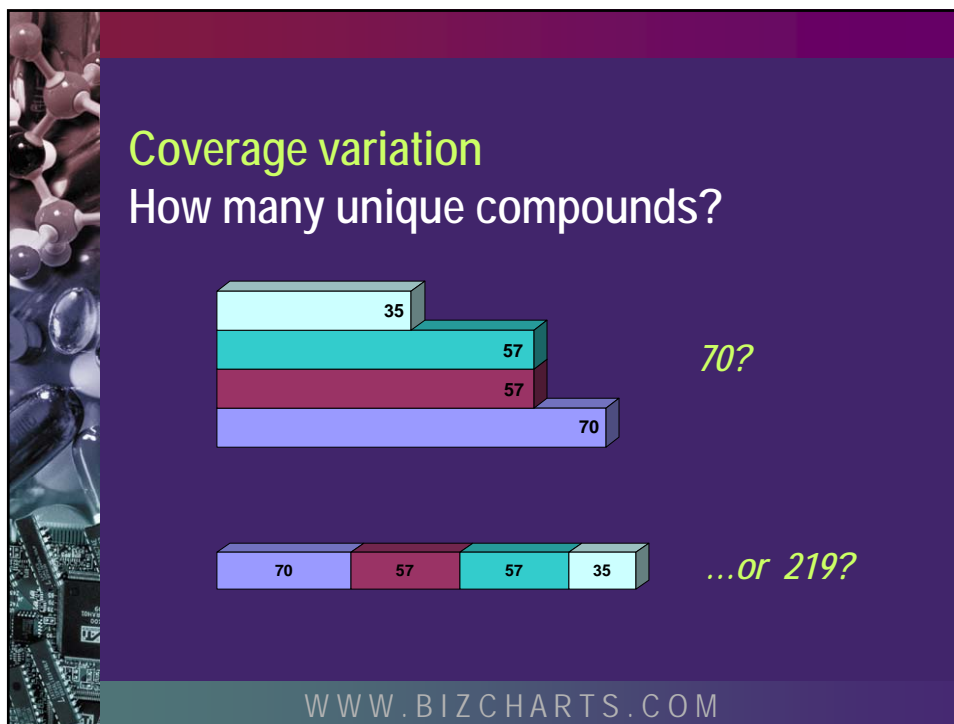



Coverage Variation

Case study 1: Amgen pipeline (Jan 02)

- **Search = "originator or licensee is Amgen"**
- Pharmaprojects 70 records
- R&D Focus 57 records
- R&D Insight 35 records
- IDdb 57 records

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Coverage Variation

Case study 2: Epilepsy drugs (Aug 02)

- **Search strategy:** "Therapeutic activity code =N3A" (PP, RDF, RDI)
- "Indication = epilepsy" (IDdb)

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Coverage Variation

Case study 2: Epilepsy compounds

- Pharmaprojects 407 records
- R&D Focus 202 records
- R&D Insight 201 records
- IDdb 250 records
- *Also searched Prous Drug Data Report --
2880 records retrieved*

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Coverage variation

Identifying unique compounds

	Product	Common Drug Name	Synonyms	Database
294	Diastat	Diastat		Current Drugs IDdb
295	Diazepam rectal gel	Diastat	Diastat	Adis R&D Insight
296	diazepam, Elan	Diastat	Diastat diazepam rectal gel, Elan diazepam rectal gel, Draxis	PJB Pharmaprojects

"Generate Common Drug Names" tool automatically matches product names and synonyms

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Identifying unique compounds

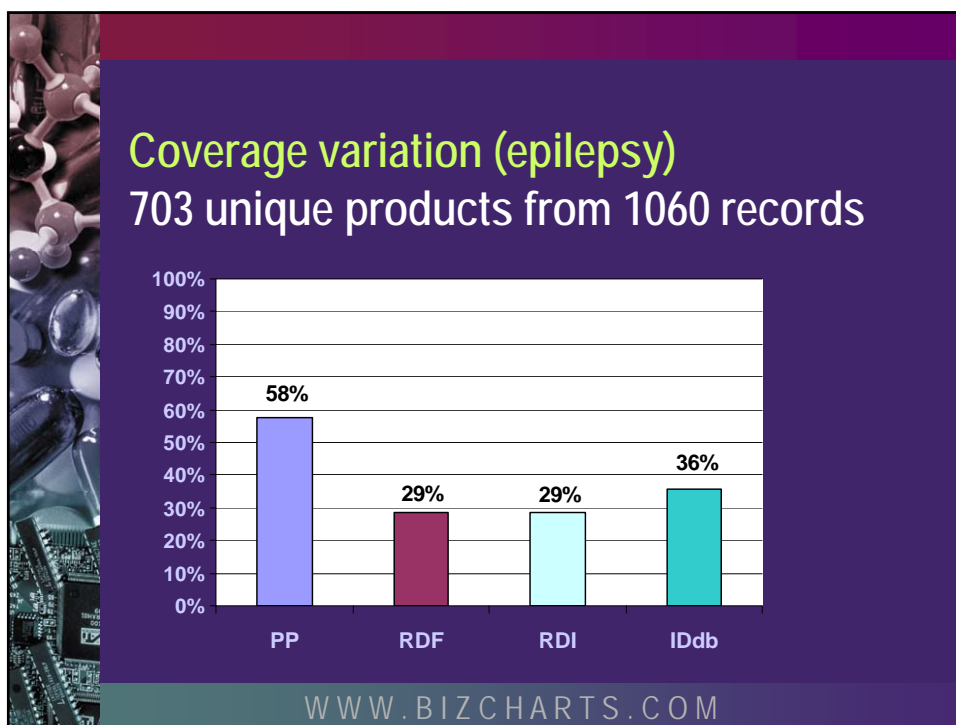
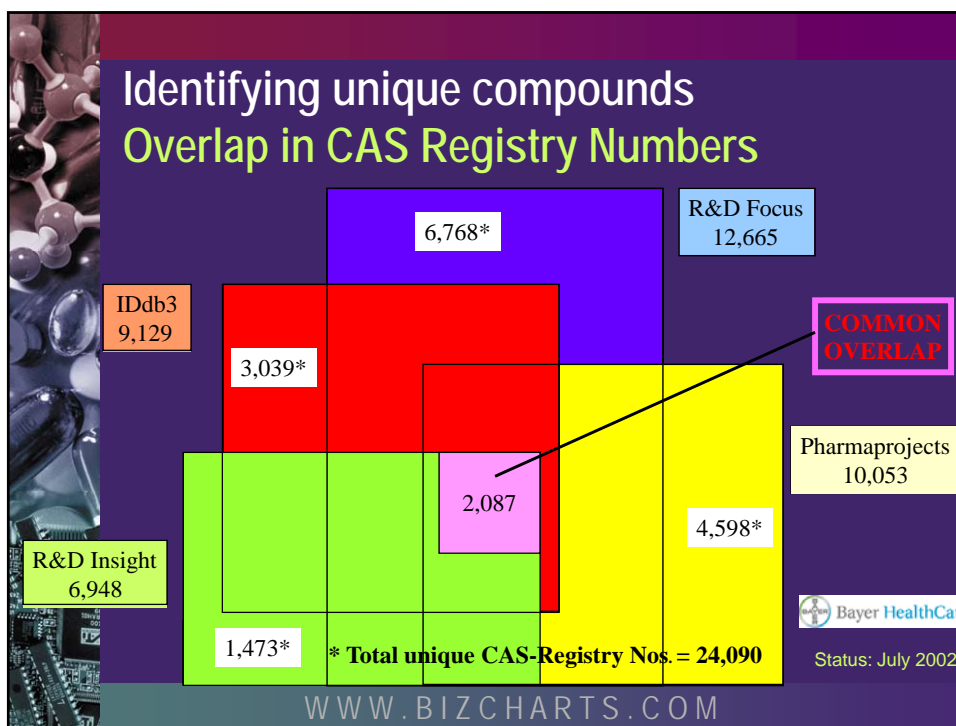
Using CAS Registry Numbers

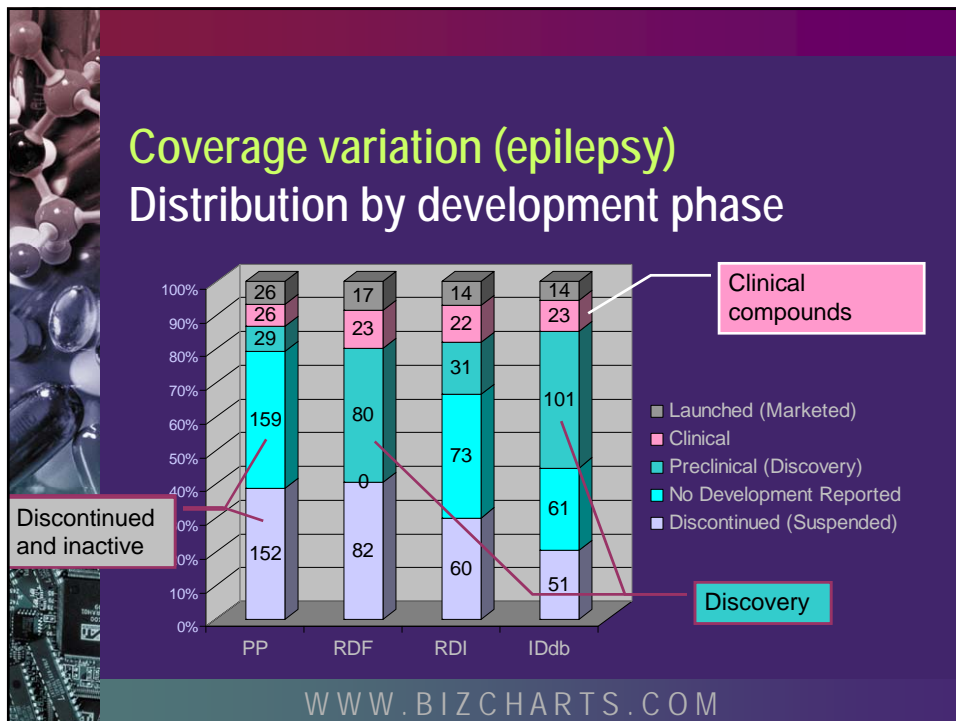
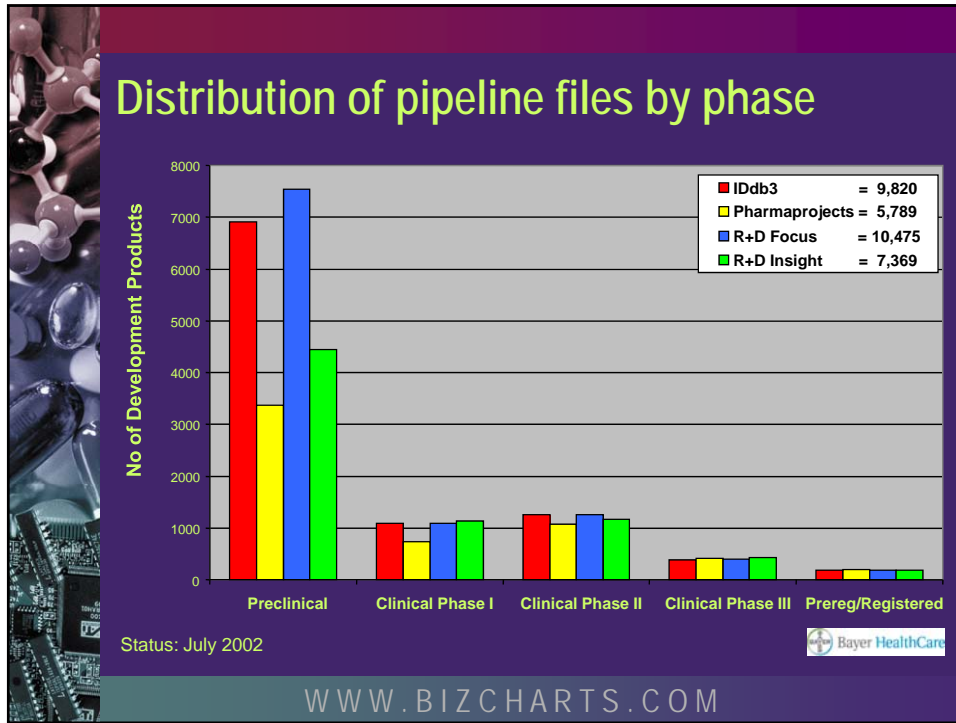
Database	Records with CAS Reg. Nos.	Total Records
IDdb3	9,130	18,939
Pharmaprojects	10,358	28,087
R+D Focus	5,145	16,177
R+D Insight	7,522	15,609

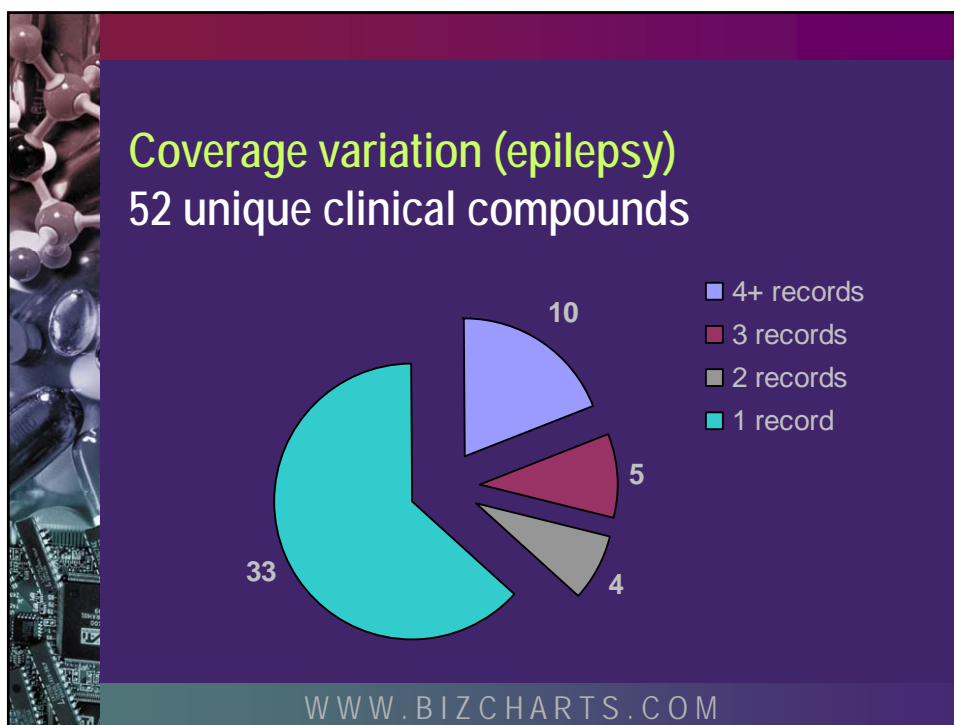
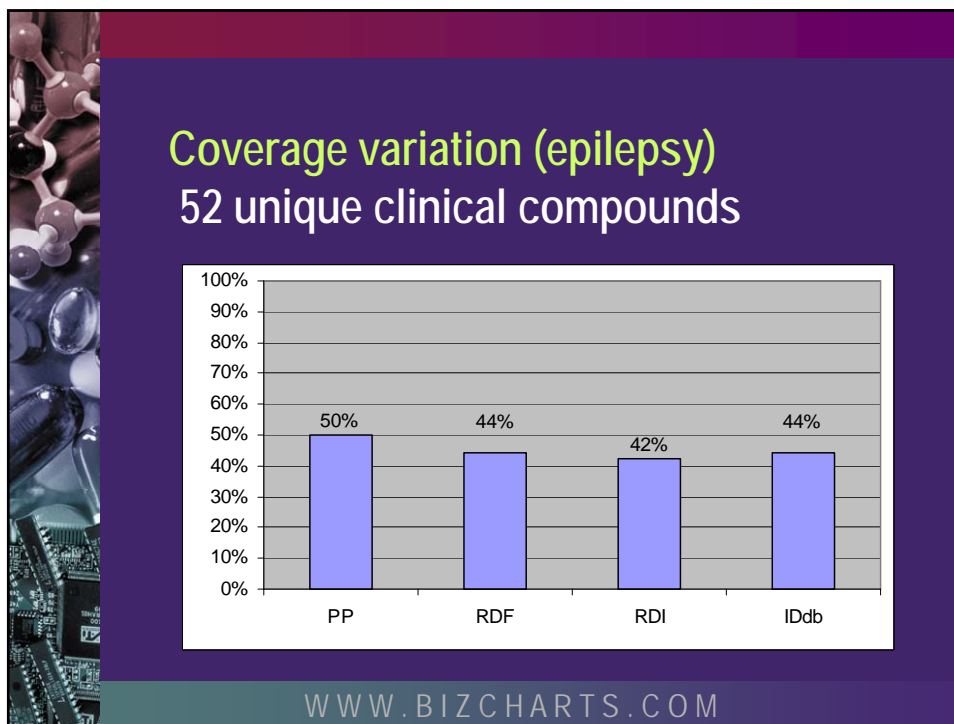
Status: July 2002

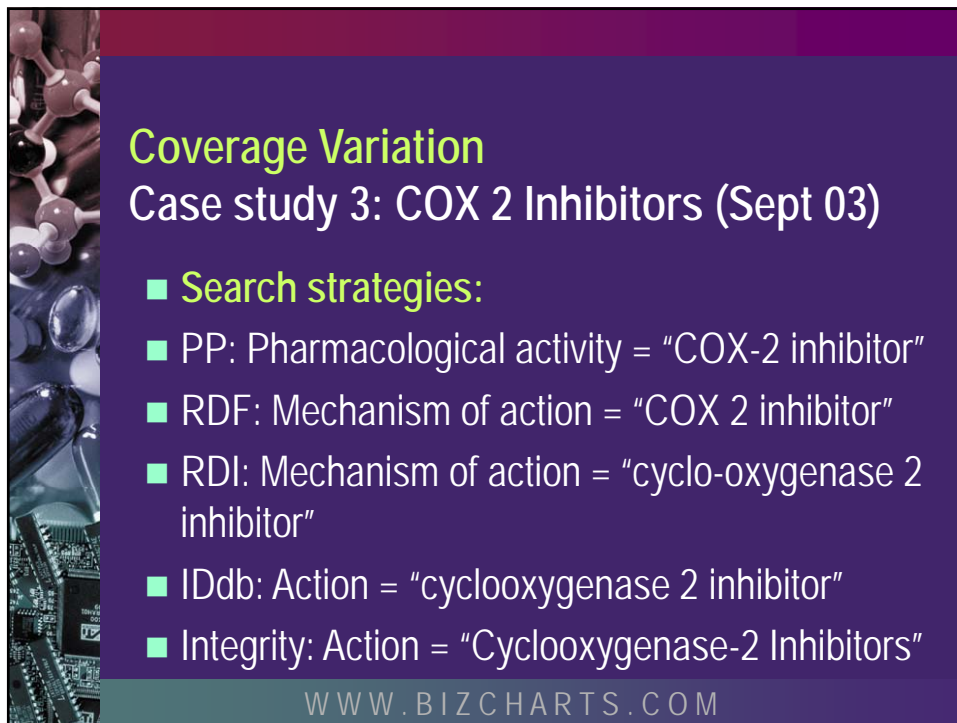
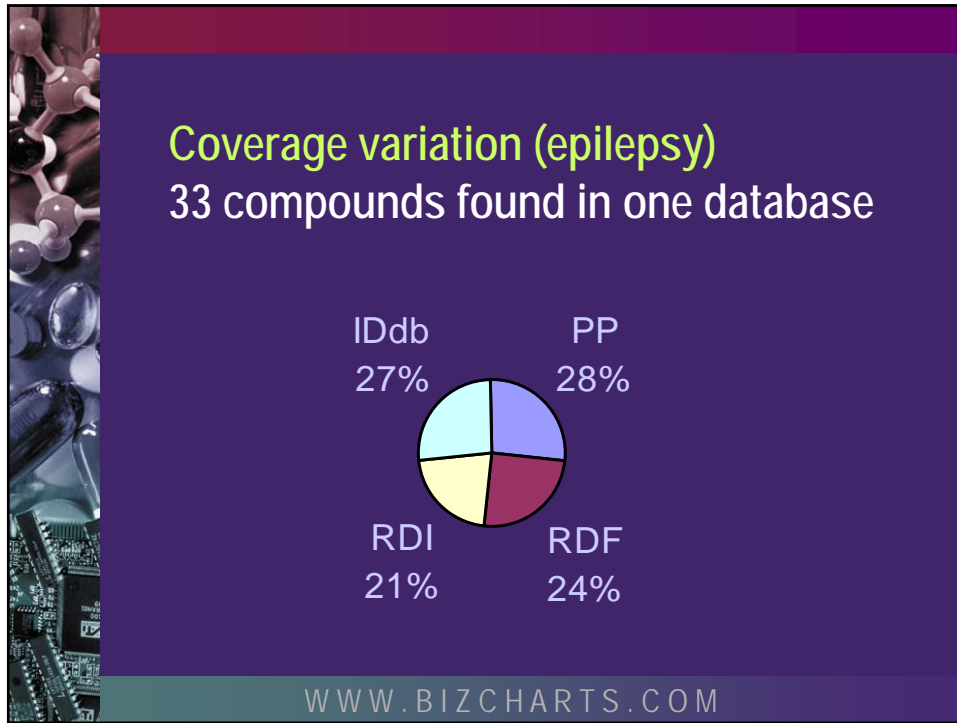
Bayer HealthCare
Published in ONLINE, May/June 2003.

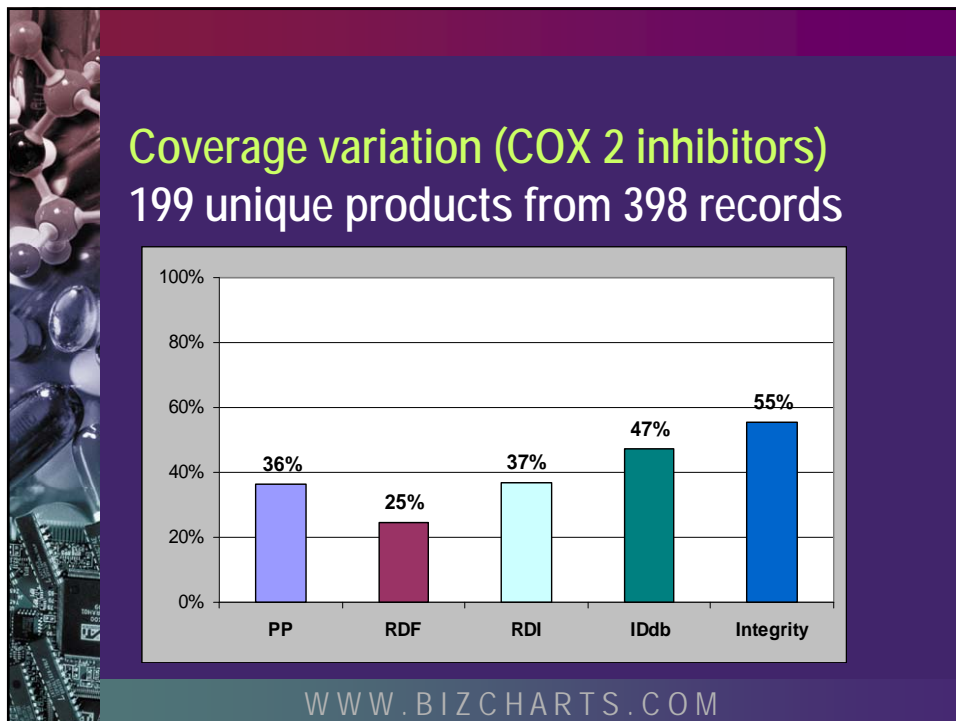
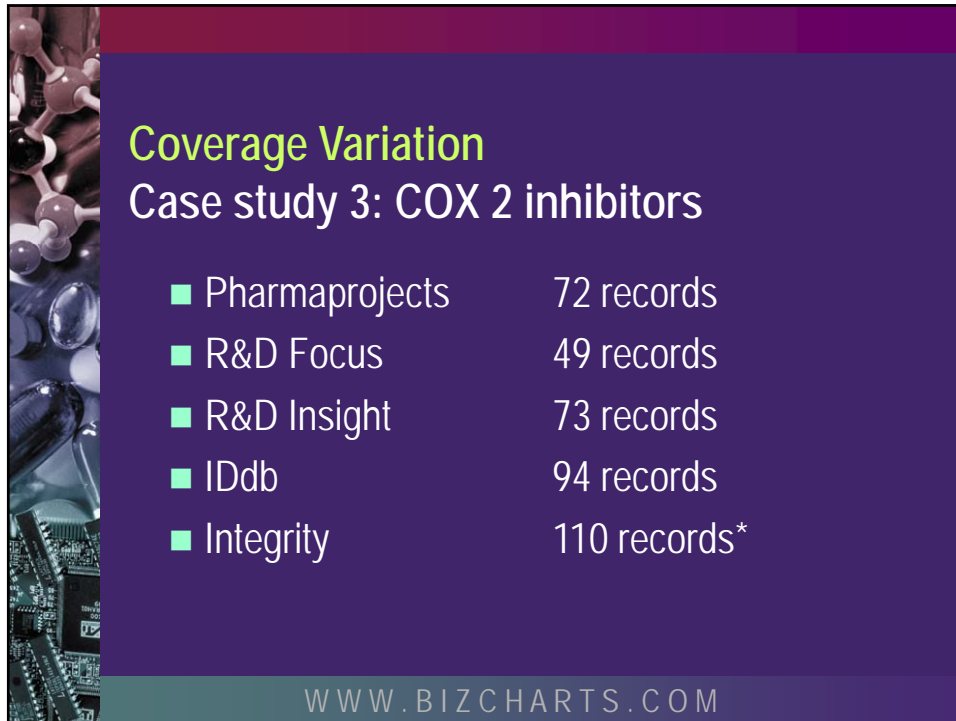
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Coverage variation - conclusions
Only a fraction of total compounds will be retrieved from any one database

- A search of any one database will retrieve about 40% of the unique compounds.
- The number of unique compounds will be roughly half the total number of records retrieved.


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Coverage variation - conclusions
Over half the compounds will be retrieved from only one database

- Compounds (esp. in discovery) can be assigned *very* different names.
- Possible that similar compounds were not matched.
- Key reason: the search missed compounds due to **indexing** variations.

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Coverage variation - conclusions

Variations in indexing result in much of the coverage variation

- Alfimeprase: doesn't appear in R&D Insight
- CNTF: RDI record doesn't mention Amgen
- Abelcet (ABLC): IDdb record mentions Amgen, but not indexed by Amgen
- KRN-568: Indexed as Kirin & NPS in Pharmaprojects

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Coverage variation - conclusions

Compounds are usually in all databases, but are not retrieved by the search

- **Sanofi-Synthelabo analysis by Bayer**
- Preclinical: of 30 records in IDdb, 15 were in the other 3 files.
- Phase I: 10 records in IDdb; all in other 3.
- Phase II: 12 records in IDdb; 10 in other 3.
- Phase III: 6 records in IDdb; all in other 3.

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Coverage variation - conclusions

A database may contain multiple records for the same compound

	Drug	sc name	Database	Synonyms	Status	CAS Number
1	ersofermin	ersofermin	Current Drugs IDdb		No Development Reported	
2	fibroblast growth factor, Amgen	ersofermin	Current Drugs IDdb		No Development Reported	
3	ersofermin (INN)	ersofermin	IMS R&D Focus	fibroblast growth factor, basic basic fibroblast growth factor bFGF TROFAK	Suspended	111212-85-2
4	fibroblast growth factor, basic	ersofermin	IMS R&D Focus	bFGF	Suspended	
5	ersofermin	ersofermin	PJB Pharmaprojects	angiogenesis factor, Synergen bFGF, Synergen bFGF, Syntex FGF, Synergen FGF, Syntex fibroblast growth factor, Syn Trofak	Discontinued	111212-85-2
6	fibroblast growth factor, Amg	ersofermin	PJB Pharmaprojects	FGF, Amgen	No Development Reported	62031-54-3

Two records from each of three databases

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Content Variation

Lexigen pipeline (Dec 01)

	Drug	Database	Originator	Highest Phase	Therapeutic Class (EphMRA)	Mechanism Of Action	Last Update
1	FP-21399	PJB Pharmaprojects	Merck KGaA (Germany)	Phase II Clinical Trial	Antiviral, anti-HIV (J5A)	GP120env antagonist (GP-120-AN)	1999-03-23
2	FP 21399	IMS R&D Focus	Fuji Photo Film (Japan)	Phase I	Other HIV Antivirals (J5C9)		2001-07-01
3	FP 21399	Adis R&D Insight	Lexigen Pharmaceuticals (USA)	Phase II	HIV antivirals (J5C)	HIV fusion inhibitors	2001-07-11
4	FP-21399	Current Drugs IDdb	Lexigen Pharmaceuticals Corp	Phase 2 Clinical		V3 loop cleavage inhibitor	

Different Originators
Different Phases
Update Dates

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Content Variation Phase of development

RDI and RDF list compound in Phase I, PP and IDdb list in Phase II

	Product	Common Drug Name	Database	Synonyms	Highest Phase	Last Update
	AMP 397A	AMP-397	Adis R&D Insight		Phase I	2000-04-14
4	AMP-397	AMP-397	PJB Pharmaprojects	AMP-397A	Phase II Clinical Trial	2002-02-07
5	AMP 397	AMP-397	IMS R&D Focus		Phase I	2001-10-08
6	AMP-397A	AMP-397	Current Drugs IDdb		Phase 2 Clinical	2002-01-01

Update Dates range from April 2000 to February 2002


Content Variation Originator indexing

Original research by IDR (subsidiary of IVAX)

Licensed to Lilly

	Product	Common Drug Name	Database	Originator	Last Update	Commercial Intro
81	talampanel	talampanel	PJB Pharmaprojects	IVAX (US)	2001-06-14	Talampanel (LY-300164) is a non-competitive antagonist of the AMPA- subtype of glutamate receptors, under development by the Institute for Drug Research (IDR) (IVAX) as an antiparkinsonian, anticonvulsant, anxiolytic and neuroprotective. It is licensed to Lilly (Company communication, IDR, Feb 1998) and Lilly has entered into an exclusive agreement with IVAX, whereby IVAX will acquire worldwide development and marketing rights (Press release, IVAX, 7 Feb 2001).
	talampanel	talampanel	Current Drugs IDdb	Eli Lilly & Co	2001-12-12	IVAX is developing talampanel (LY-300164), an analog of GYKI-52466 (qv), and a non-competitive AMPA receptor antagonist, as a potential treatment for epilepsy and cerebrovascular ischemia. In February 2001, IVAX entered into an exclusive agreement with Eli Lilly to develop and market talampanel worldwide [398172]
83	talampanel	talampanel	IMS R&D Focus	Institute for Drug Research (Hungary)	2002-07-29	Talampanel originated from research conducted at the Institute for Drug Research (IDR, Hungary), a wholly owned subsidiary of IVAX. It was licensed out to Lilly, however, following the acquisition by IVAX of IDR, IVAX signed an agreement to acquire worldwide rights from Lilly (IVAX, FEB 2001). [CONT.]


Rights re-acquired by IVAX



Coverage and content
Why is there so much variation?

- Drug pipeline records are not abstracted from a reference document (as with patents)
- Each record is an **editorial view** of the compound based on a range of sources.

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Coverage and content
Information sources can be misleading

- "As a disclosure of compound information is balanced by the business need to maintain competitive advantage, some compound information has not been disclosed at this time."

-- AstraZeneca website
(as reported by Alexander Mullin, Bayer)

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Coverage and content

Why is there so much variation?


- Publishers differ in background and focus.
- Editors assigned by therapy or company -- vary in experience and skill.
- Different update schedules
- Different index vocabularies
- Unique content (e.g. Lehman data in RDI).

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PJB Pharmaprojects

Background



- PJB: named for founder Philip J. Brown; based in Richmond (outside of London)
- PJB's best known product is *Scrip*.
- The first pipeline database (1980?) -- originally published in books.
- Contains 26,000 compounds -- 6,000 active.

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PJB Pharmaprojects Sources (see PJB web site)




- Direct contact with pharmaceutical companies.
- Editors attend scientific conferences and scan abstracts.
- Review journals, newsletters, magazines, press releases, analyst and company reports.
- *Scrip* and patent publications.

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PJB Pharmaprojects Unique features



- Historical record of discontinued products and launched products.
- PJB ratings.
- PJB therapy codes.
- Structured mechanism of action coding.

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IMS R&D Focus Sources




- "Data is gathered through direct contact with manufacturers and research organisations. It appraises both the scientific and commercial aspects of drug development."

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IMS R&D Focus Unique features



- First to cover devices, delivery systems, etc. (no longer unique, but still a strength)
- Coverage of international patents (from Drug Patents International database)
- Good biotechnology coverage

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Levitra (Vardenafil) Record R&D Focus

Scientific Summary:
 Phosphodiesterase 5 (PDE5) inhibitors have been shown to be effective in the treatment of erectile dysfunction (ED). The proposed vardenafil hydrochloride (Levitra) is a novel PDE5 inhibitor which is expected to be more effective than sildenafil (Viagra) and tadalafil (Cialis) in the treatment of ED. Vardenafil is a potent and selective PDE5 inhibitor which is expected to be more effective than sildenafil and tadalafil in the treatment of ED. Vardenafil is a potent and selective PDE5 inhibitor which is expected to be more effective than sildenafil and tadalafil in the treatment of ED. Vardenafil is a potent and selective PDE5 inhibitor which is expected to be more effective than sildenafil and tadalafil in the treatment of ED.

Date	Event	Location
2003-09-12	Phase 3 Approval	USA
2003-09-12	Phase 3 Approval	Canada
2003-09-12	Phase 3 Approval	UK
2003-09-12	Phase 3 Approval	France
2003-09-12	Phase 3 Approval	Germany
2003-09-12	Phase 3 Approval	Italy
2003-09-12	Phase 3 Approval	Spain
2003-09-12	Phase 3 Approval	Japan

Status: Sept. 2002

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Adis R&D Insight Background

- Adis International is based in New Zealand (founded by two Australian doctors)
- Third pipeline database (1995?)
- Spinoff of Adis' clinical trials database (Literature Monitoring Service (LMS) - now Clinical Trials Insight)
- 16,000+ compounds



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Adis R&D Insight Sources




- Scientific journals (trials reviewed by CTI staff)
- conferences
- industry intelligence
- Adis drug information database

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Adis R&D Insight Unique features



- Strongest when drugs are in clinical trials
- Links to reviewed trials in CTI
- Lehman Brothers commercial/sales estimates
- Adis ratings

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Levitra (Vardenafil) Record - R&D Insight




The screenshot displays a detailed drug record for Levitra (Vardenafil). It includes a chemical structure, a table of clinical trial phases (Phase I, II, III), and various text sections such as 'Description', 'Indications', and 'References'. The record is dated 'Status: Sept. 2002' and features the Bayer HealthCare logo.

Status: Sept. 2002




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Current Drugs IDdb Background




- Current Drugs is part of the Current Science group; headquartered in London.
- Newest pipeline database (late 90's)
- Started with in-house database system; now delivered over Internet.
- 17,000+ "investigational drugs"

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Current Drugs IDdb Sources




- Scientific meetings (use consulting scientists as well as staff)
- Scientific literature (link to EMBASE, MEDLINE)
- Patents (part of the DrugNet database)
- Company communications, annual reports, and press releases.

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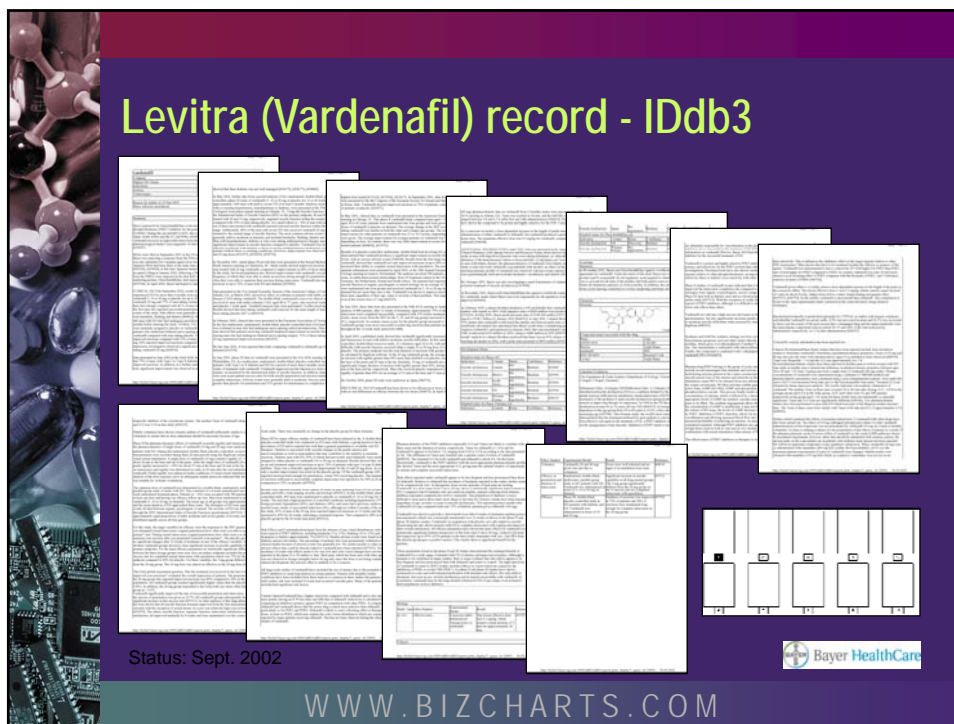


Current Drugs IDdb Unique features



- Updated daily; internet only -- hypertext interface
- Heavy patent coverage
- "real" chemical structures
- Current Drugs policy limits export to any platform to only a few fields: Product, Company, Status, Indication, Action, Technology, Patent.

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Levitra (Vardenafil) record - IDdb3

Status: Sept. 2002

Bayer HealthCare

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Surfing the drug pipeline

Keep in mind...

- Significant variations in coverage and content.
- Differences are a natural result of editorial process.
- Data from any one database will likely be incomplete and inaccurate.
- **Search as many databases as you can!**

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Surfing the drug pipeline

Keep in mind...



- **The good news:** can leverage of work of dozens of researchers and editors.
- **The bad news:** must resolve the differences between these experts.
- **Develop your own editorial policy for drug pipeline data!**

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