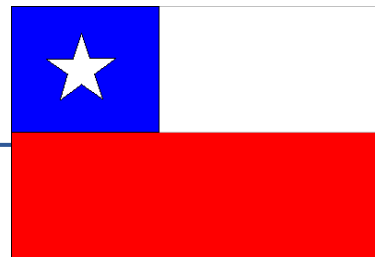


THE IMPACT OF FOREIGN PHARMACEUTICAL PATENTS ON INNOVATION IN CHILE



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India's Glivec decision, 1 April 2013

- Novartis's patent application on Glivec (Gleevec, generic imatinib, an effective anti-cancer drug) in India rejected by Supreme Court for obviousness
- Crucial issue: are new forms (beta crystalline form) of known substances (imatinib mesylate) patentable?
- Original discovery of imatinib goes back to 1993
- Novartis's reaction: will be "cautious" about introducing new drugs to India, undertaking new investments, and conducting R&D in India...

Current policy debate

- Proposals to restrict secondary patents:
 - **Brazil's** Projeto de Lei n° 5.402/2013 (includes provision similar to paragraph 3d of India's Patent Act).
 - **South Africa's** proposed National Policy on IP: “[Legislation] should exclude diagnostic, therapeutic and surgical methods from patentability, including new uses of known products, as is the case under the TRIPS agreement.”
 - **TPP's** draft Article QQ.E.1: critical issue - patentability of new uses or methods of using a known product and “enhanced efficacy of a known product” threshold.

The big questions...

- Pharmaceuticals often important argument for strengthening of Intellectual Property (IP) system in developing countries
- Does stronger patent protection promote:
 - The decision by foreign multinationals to sell drugs in developing countries? *Yes, according to Cockburn, Lanjouw, Schankerman*
 - Technology transfer to developing countries? *Maybe not*
 - Foreign direct investment? *Probably*
 - The development of a domestic, innovative pharmaceutical industry?

Our study

- Exploratory, based on a complete set of data for a single country, Chile.
- Ingredients:
 - Complete **patent** application database, including applicant info, legal status, etc., 1991-2010
 - Complete **trademark** application database with the same, 1991-2010
 - Complete list of **drugs registered** at the ISP (Institute of Public Health) 1934-2012, with owners and producers, active ingredients, etc.
- Many challenges in matching these data, and this is work in progress
- Current paper is a *tour d'horizon* that maps out the landscape

Our Research Questions

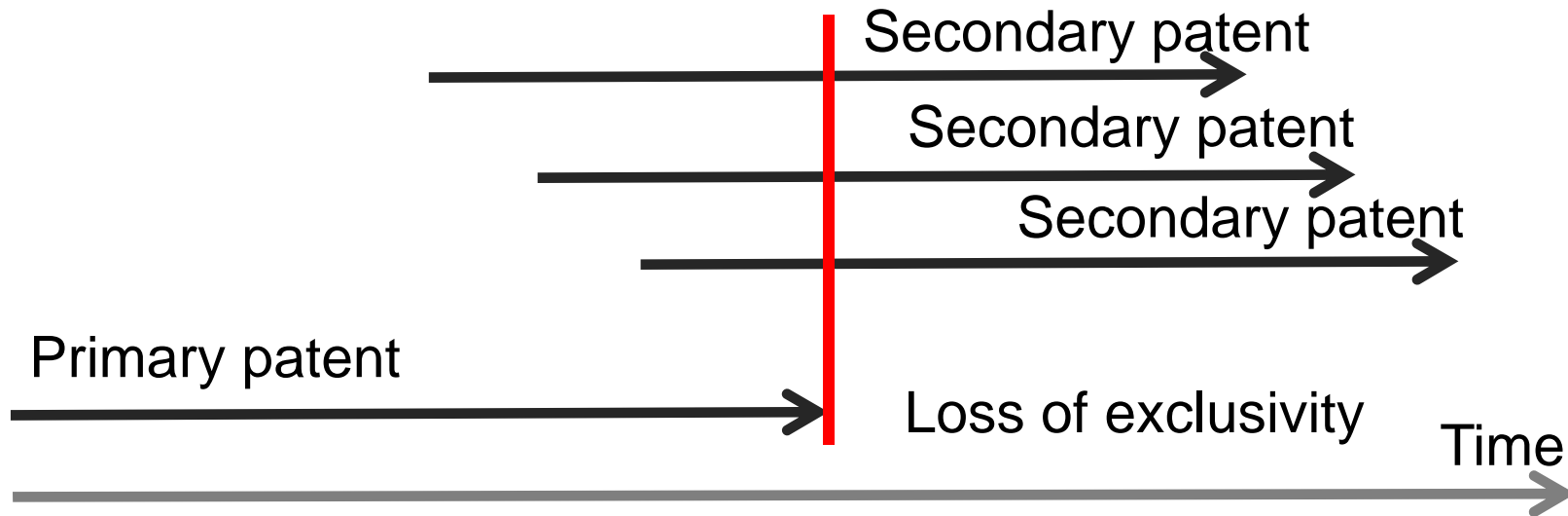
- What is the share of patents held by foreign pharma companies associated with drugs commercialized on the domestic market?
 - This measures “working” of patents
- Do foreign pharma firms use strategic patenting behavior to keep domestic generic producers off the market?
 - This measures impact on (broadly defined) “innovation”
 - More specifically:
 - How is entry into the manufacture of drugs for specific therapeutic categories affected by the presence of foreign pharma patents?
 - Do secondary patents delay entry by Chilean firms into drug production

Patenting strategies

- Multiple functions of patents: ensure freedom to operate, bargaining etc
- Are patents also used to block/delay entry of generics and avoid loss of (broad) exclusivity?
- Primary vs secondary patents
 - Extend patent life
 - Increase patent breadth
 - Facilitate follow-on inventions (“evergreening”)

Patenting strategies: length

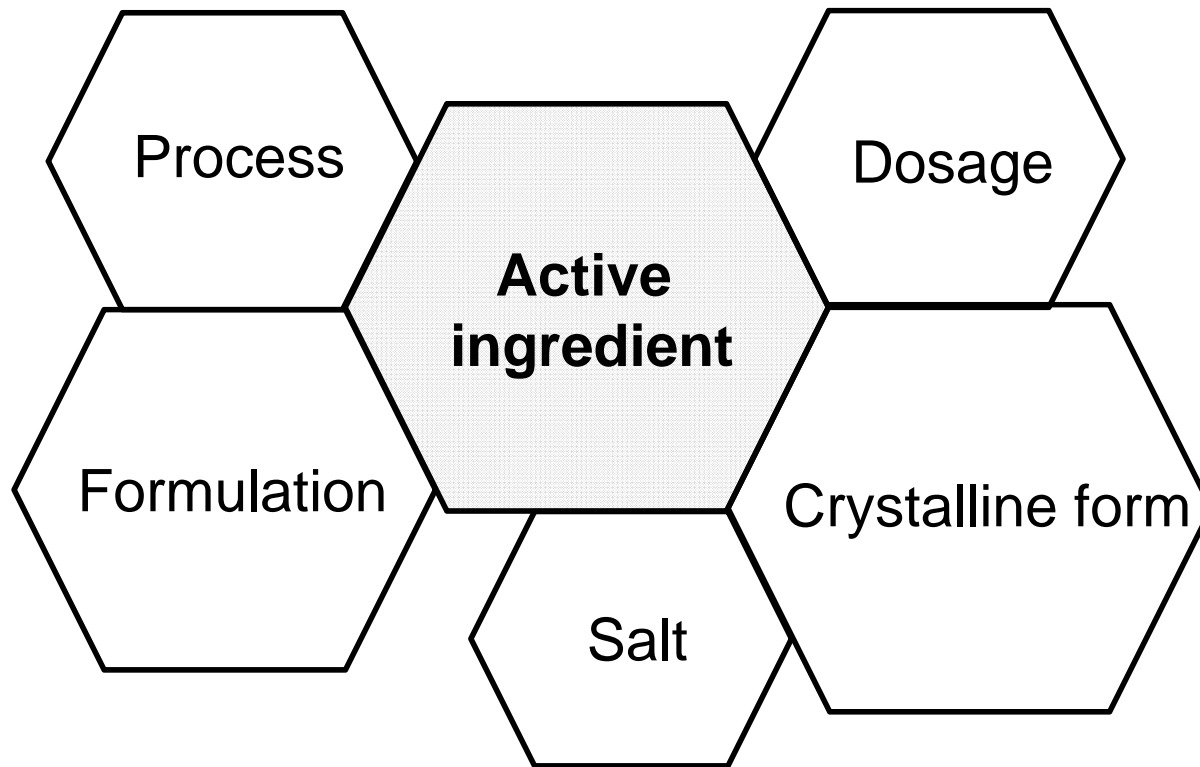
- Patent cluster to extend lifetime



- Incremental innovation or fencing strategy?

Patenting strategies: breadth

- Patent cluster to extend breadth:



- Incremental innovation or fencing strategy?

Patenting strategies: anecdotal evidence

"We were recently successful in asserting the crystalline form patent in [name of country], where we obtained an injunction against several generic companies based on these patents by 'trapping' the generics: they either infringe our crystalline form patent, or they infringe our amorphous form process patent when they convert the crystalline form to the amorphous form."

Anonymous pharmaceutical company quoted in EU Commission (2009)

"The entire point of the patenting strategy adopted by many originators is to remove legal certainty. The strategy is to file as many patents as possible on all areas of the drug and create a 'minefield' for the generic to navigate. All generics know that very few patents in that larger group will be valid and infringed by the product they propose to make, but it is impossible to be certain prior to launch that your product will not infringe and you will not be the subject of an interim injunction."

Anonymous generic producer quoted in EU Commission (2009)

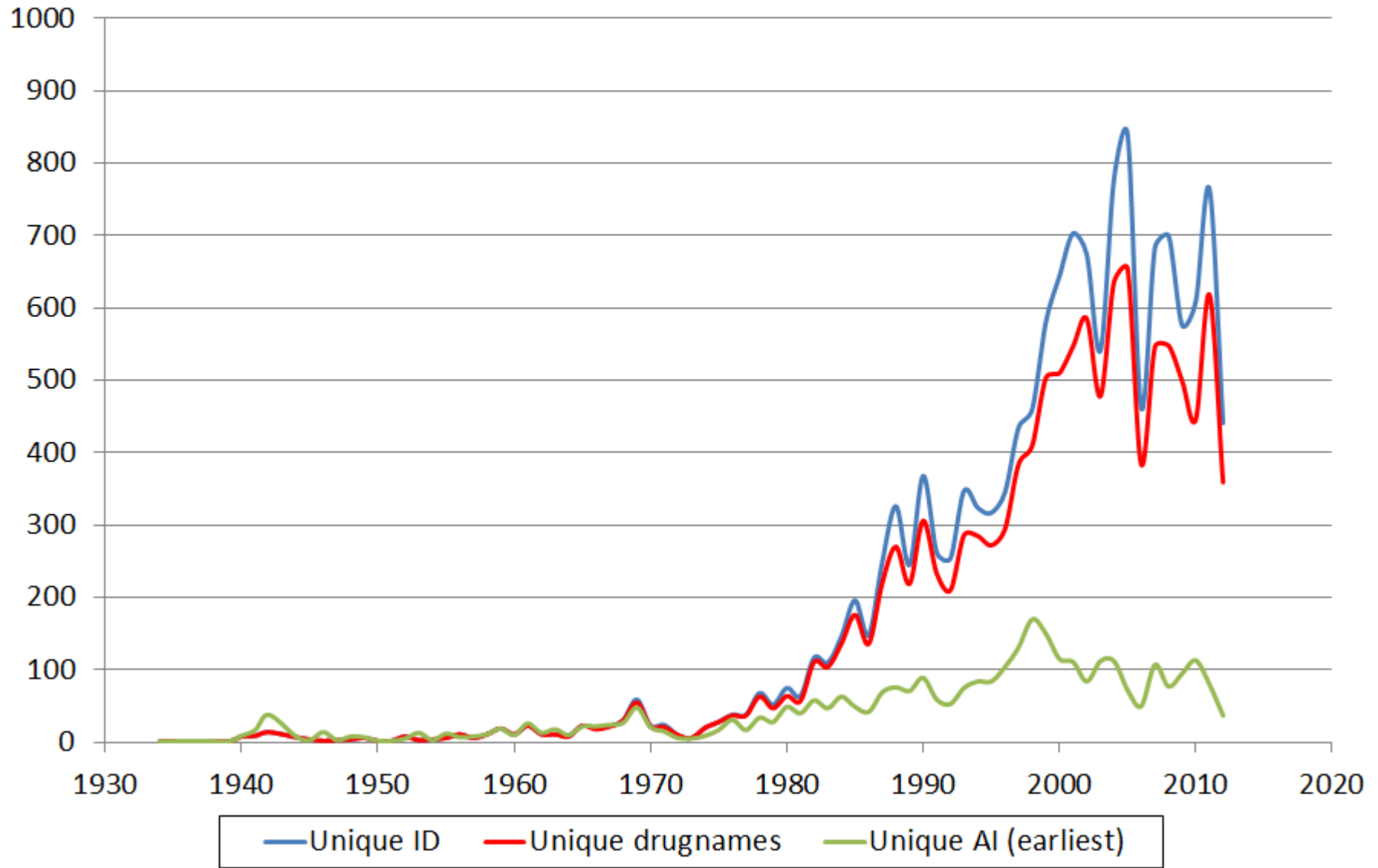
Patenting strategies: empirical evidence

- EU Commission (2009):
 - primary to secondary patent ratio 1:7
 - pending patents 1:13
 - granted patents 1:5
 - Disproportionately more secondary patents after product launch
- Kapczynski et al. (2012):
 - Of new drugs with FDA in 1991-2005: 56% formulation, 24% salts, crystalline forms etc., 63% methods of use (secondary patents)
 - Secondary patents filed after FDA approval and extend exclusivity lifetime by 4-5 years
 - More secondary patents the higher is the branded drug's sales

Chilean setting - ISP

- Midlevel developing/emerging economy with relatively good institutions
- Drugs must be registered with the Public Health Institute (ISP)
 - Submit samples, formulae, clinical trial evidence
 - Takes 6-18 mos, fees are ~\$2300
 - Many registrations are for new formulations of existing drugs
 - Generics can rely on proprietary evidence after 5 years of exclusivity following ISP application
 - now changing to require proof of bioequivalence
 - Patent protection not required for registration

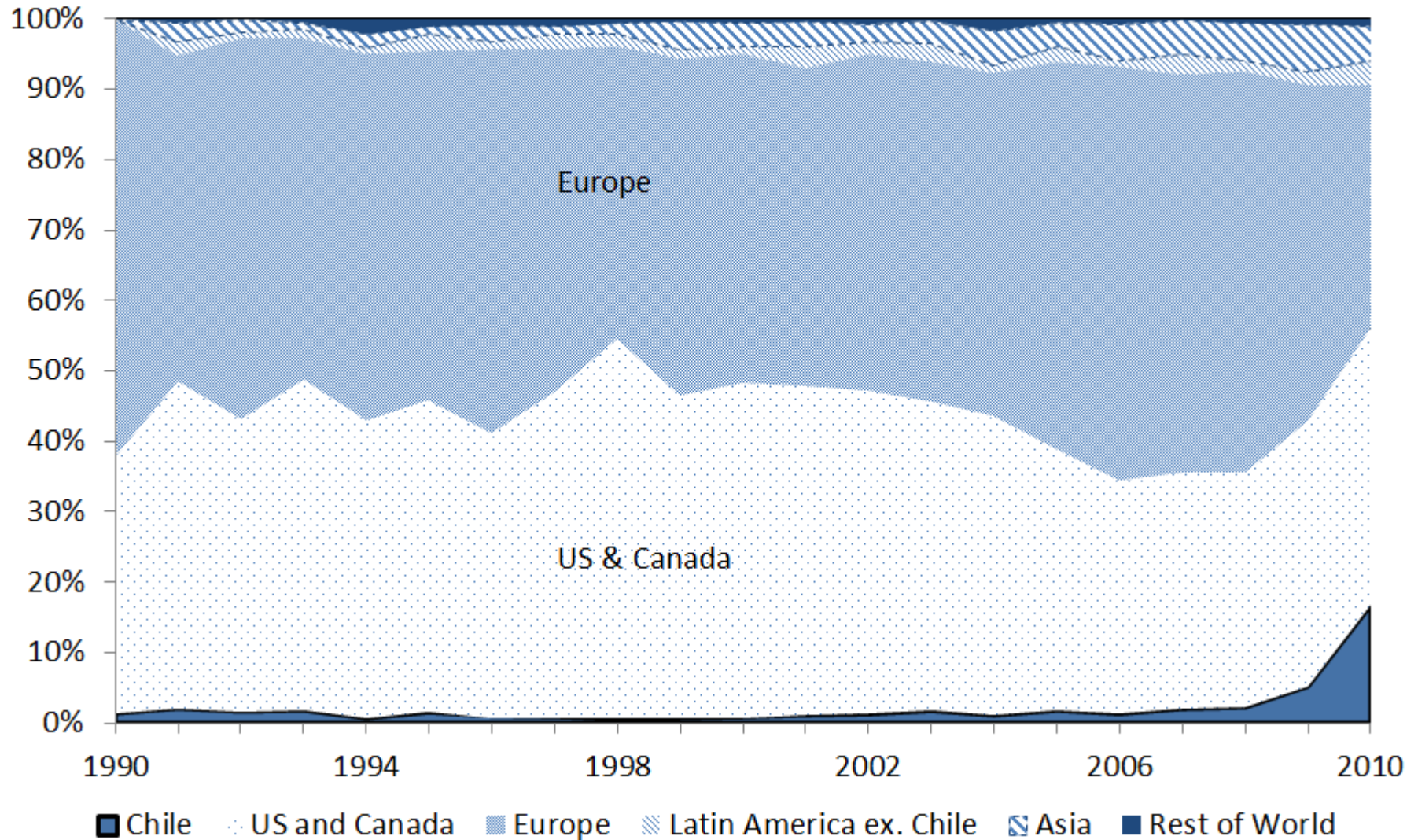
Registrations (ID), products (drugs) and active ingredients (AI) registered at the Chilean ISP



Chilean setting – pharma patents

- Patents
 - Joined Paris convention in 1991
 - Joined PCT in June 2009 (very late in our data)
- Pharmaceutical patents
 - Not allowed until 1991; consistent growth since then
 - Excluded coverage for all patents applied worldwide before then for pharma
 - Law amended several times to bring in line with TRIPS and FTA/EFTA
 - Extend life from 15 to 20 years
 - Allow for extension due to delays in grant/registration
 - Softening of secondary use restriction
 - Etc
 - Only a small fraction (<2%) held by Chilean entities; largest source countries are US, Switzerland, Germany

Total pharmaceutical patent filings by domestic and foreign entities in Chile



Data Construction

- Objective: link products with patents & trademarks
- Chilean patent office (INAPI): Universe of patents and trademarks filed with INAPI between 1991 and 2010 by domestic and foreign entities.
- National public health institute (ISP): All drugs registered in Chile. The information includes active ingredients of all registered products, the owner of the drug, whether the drug is produced domestically or abroad, etc. (*but not patent numbers*)
- Merck Index (MI) and US FDA Orange Book (OB): MI provides first filing of patent protecting active ingredients. OB provides US patents of active ingredients.

Data challenges

- Active ingredients, patents, trademarks use different classification systems
- A single patent can protect multiple active ingredients (and vice versa)
- A product can be associated with several patents and trademarks
- Active ingredients appear in multiple products
- Spelling of the owner name varies considerably within and across the various data sources

Data construction

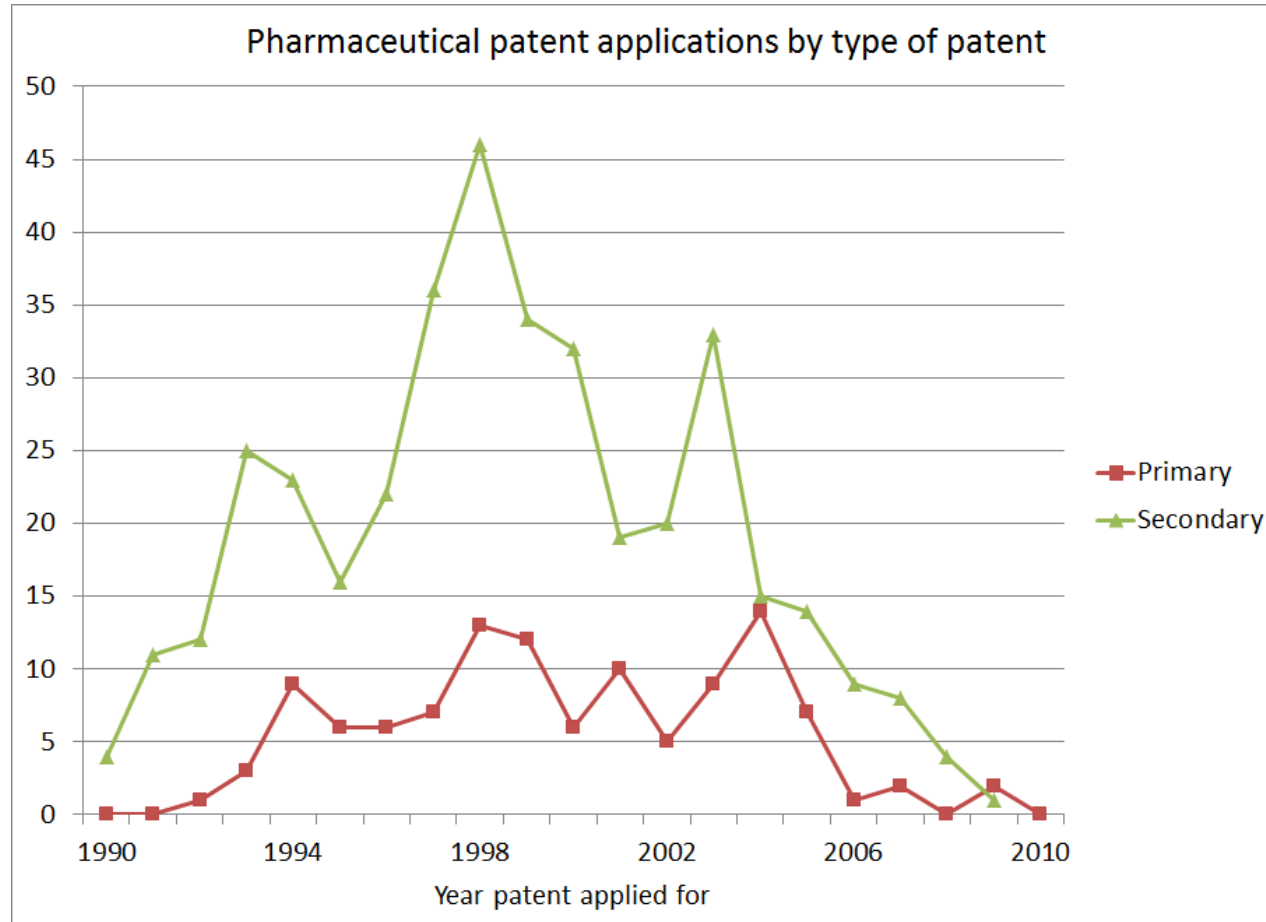
- We have an active ingredient-product match from ISP (non-unique in some cases)
- Matching CL patents to active ingredients:
 - 2005-2010: we have a match done by patent examiners specializing in pharma
 - Pre-2005: translate AI description to English; search in [Merck Index](#) of first filings and the [US Orangebook](#) for US patents associated with the AI; find CL equivalent patents;
 - Also do our own search in CL granted patents
 - All matches validated by Chilean experts in pharma patents; [they also labelled patents as secondary vs primary.](#)
- Matching CL trademarks to products
 - Search by product (drug name) and owner in the trademark database – in contrast to patents, about half of drug-associated trademarks are owned by Chilean firms

ISP registrations

	Total	Matched to patents	Share matched	Matched to trademarks	Share matched
ISP registrations	14,504	4,304	30%	9,695	67%
Unique product names	12,116	3,709	31%	9,273	77%
Unique active ingredients	2,630	322	12%	2,332	89%

Many registrations and active ingredients are for OTC medicines, vitamins, and herbal supplements.

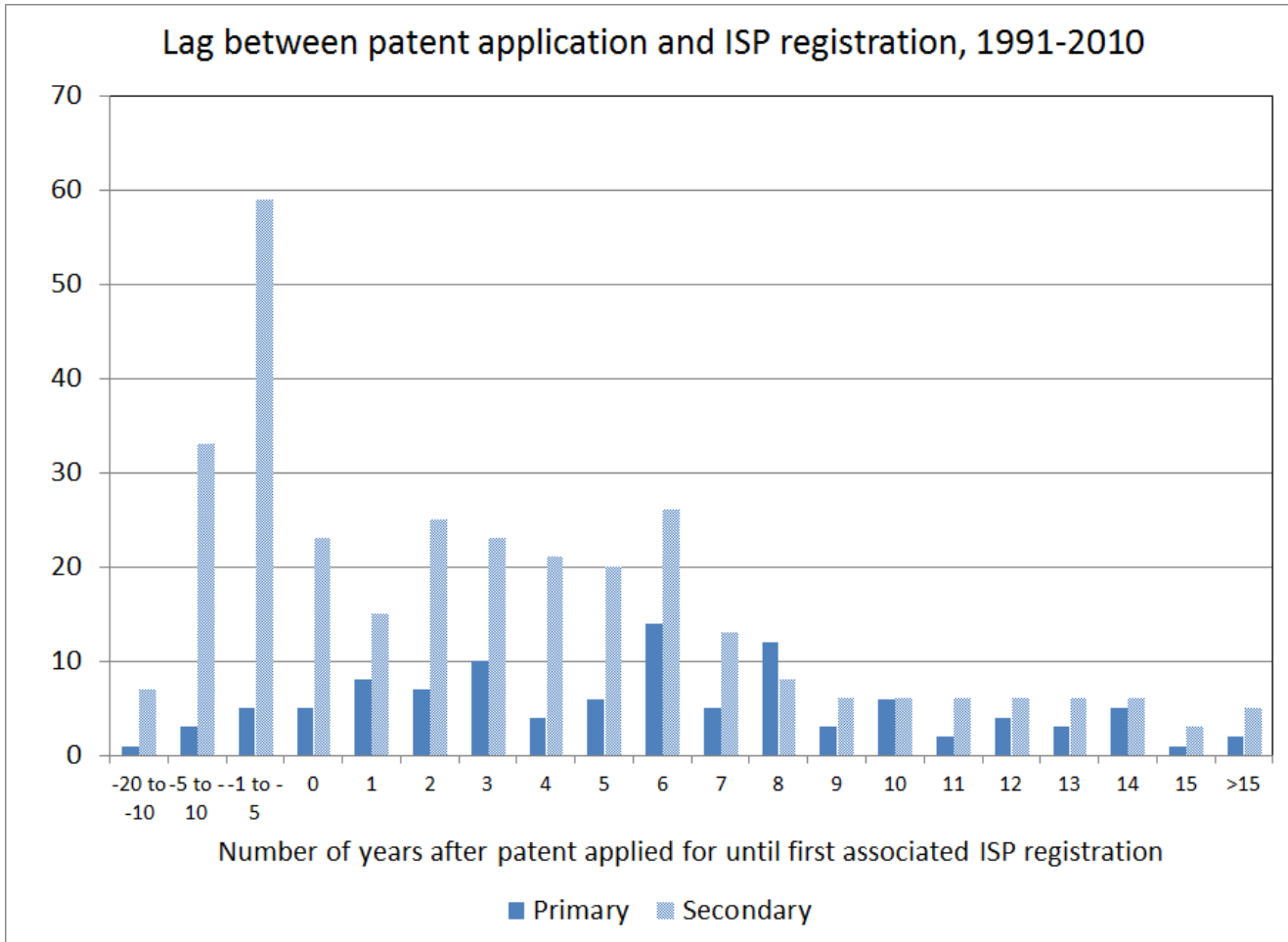
Primary vs secondary patents



113 (22%) of 504 matched patents are primary patents.

Primary pats more likely to have been granted.

Does ISP registration lag patent app?



86% of primary patents applied for before ISP registration.

56% of secondary patents applied for before ISP registration.

Median lags:

Primary - 6 years

Secondary - 2 years

Delayed entry?

Top therapeutic classes protected by patents

- Anti-ulcer, anti-depressants, etc. are older drugs (pre-1991) and have few primary patents if any.
- Anti-virals (including HIV) and anti-neoplastics (anti-cancer) are newer.

Number of patents per therapeutic class

<i>Therapeutic group</i>	<i>Number</i>		<i>Share</i>
	<i>Primary patents</i>	<i>Secondary patents</i>	<i>Primary patents</i>
anti-viral agents	20	41	32.8%
anti-neoplastics	14	23	37.8%
anti-depressants	2	33	5.7%
anti-psychotics	1	31	3.1%
anti-diabetic agents	8	24	25.0%
analgesics	8	23	25.8%
nonsteroidal anti-inflammatory agents	7	20	25.9%
immunologic agents	9	13	40.9%
antibiotics/anti-neoplastics	5	17	22.7%
gastrointestinal agents (anti-ulcer)	2	19	9.5%
anti-fungals	3	16	15.8%
broncho-dilators	1	18	5.3%
anti-asthmatic combinations	3	15	16.7%
anti-histamines	2	15	11.8%
agents for pulmonary hypertension	1	15	6.3%
bone resorption inhibitors	0	16	0.0%
quinolones	3	12	20.0%
cholesterol absorption inhibitors	3	11	21.4%
hormones	1	11	8.3%
narcotic analgesics	2	10	16.7%
anti-infectives	2	10	16.7%
remaining classes	63	421	13.0%
Total	160	814	

ISP registrations – various firm functions

	<i>Chile</i>	<i>Europe</i>	<i>Latin America</i>	<i>US & Canada</i>	<i>Rest of world</i>	<i>Total</i>
Chilean mfg - finished	11,612	6	10	1	1	11,630
Chilean mfg - bulk	76	6	6	0	3	91
Foreign mfg - finished	25	3,492	4,014	889	2,842	11,262
Foreign mfg - bulk	9	1,007	1,314	269	506	3,105
Mfg of principal AI	0	218	0	6	52	276
Quality control	16,826	2	5	0	38	16,871
Source	9	4,585	6,523	1,037	3,429	15,583
Licensor	22	4,083	1,017	1,861	543	7,526
Foreign packager	6	83	123	22	7	241
Chilean packager	2,822	0	3	0	1	2,826
Packer	3,737	169	154	23	1	4,084
Importer	9,432	0	1	0	2	9,435
Distributor	21,841	1	0	0	0	21,842
Total	66,417	13652	13170	4108	7,425	104,772

Role of Chilean firms

- Mostly domestic manufacturing, quality control, importing, packaging, and distribution
- Two drugs have a Chilean firm as the source, but no patents:
 - meropenem trihydrate (generic antibiotic)
 - warfarin sodium (generic anti-coagulant)
- Two drugs have secondary patents owned by Chilean firms, no primary patents:
 - Larmax-D, an anti-histamine compound
 - Faronkal, a nasal decongestant compound used for sleep apnea
- Regress share of Chilean firms mfg each AI on primary patent dummy, number of ISP regs for that AI, number of patents for that AI

Predicting the share of Chilean manufacturing companies for each active ingredient

<i>Method of estimation</i>	<i>OLS</i>			<i>Tobit</i>		
D (any primary patent)	-0.15	(0.04)	***	-0.42	(0.10)	***
Log (number of ISP regs)	0.05	(0.01)	***	0.17	(0.03)	***
Log (number of patents)	-0.01	(0.03)		-0.03	(0.06)	
Year dummies	insignificant			no		
Standard error	0.304			0.635		
R-squared	0.166			0.109		

381 observations

Coefficients and standard errors robust to heteroskedasticity are shown.

*** denotes significance at the 0.001 level.

The year dummies are for the year of the first associated patent application.

Doubling the number of ISP registrations increases the share mfg by Chile by 0.17

If an AI has a primary patent, lowers the Chilean mfg share by 0.42

The total number of patents associated with that AI is not related to the Chilean manufacturing share.

There is little trend.

Predicting the share of Chilean manufacturing companies within a therapeutic class

<i>Method of estimation</i>	<i>OLS</i>			<i>Tobit</i>		
Log (number of drugs)	0.045	(0.024)	*	0.084	(0.034)	**
Log (number of patents)	-0.012	(0.031)		-0.026	(0.039)	
Share of primary patents	-0.255	(0.098)	***	-0.472	(0.178)	***
D (no patents)	0.216	(0.206)		0.254	(0.326)	
Year of first pat app in class	0.0001	(0.0001)		0.0002	(0.0001)	
Standard error		0.332			0.483	
R-squared		0.068			0.055	

240 observations

Coefficients and standard errors robust to heteroskedasticity are shown.

***, **, * denote significance at the 0.01, 0.05, 0.10 level respectively

Clearly classes with primary patents see very reduced entry by Chilean manufacturers.

However, no evidence in the case of secondary patents

Conclusion

- Almost **all pharma patents** in Chile held by **foreign** firms
- Almost **no products** by domestic companies protected by patents
- **Negative** relationship across therapeutic classes between share of drugs patented by foreign companies and number of drugs by domestic companies
- Weak evidence for **strategic patenting** behavior in pharmaceuticals in the form of extending patent life
- Work in progress...