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Responsabilidades del Investigador y Conflicto de Intereses

Rodrigo A. Salinas

Departamento de Ciencias Neurológicas
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☞ Conflicto de intereses (definición)

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↳ "Conjunto de condiciones en las cuales el juicio profesional referente a un interés *primario* (tales como el bienestar de un paciente o la validez de una investigación) tiende a ser indebidamente influido por un interés *secundario* (tal como una ganancia pecuniaria)"

BMJ 1998; 317(7154): 291–292.

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DIFFERENTIATING CLINICAL TRIALS FROM MEDICAL CARE

Clinical medicine aims to provide individual patients with optimal care. The risks of diagnostic tests and treatments are justified by the prospect of compensatory medical benefits for the patient. By contrast, clinical research is devoted to answering scientific questions in order to produce generalizable knowledge. Physician-investigators conduct clinical trials to evaluate experimental treatments in groups of patient-subjects, with the ultimate goal of benefiting future patients by improving medical care. To be sure, the contrast between the group focus of clinical trials and the individual focus of medical care should not be overstated. Physicians are obligated to practice medicine in the context of a profession-

NEJM

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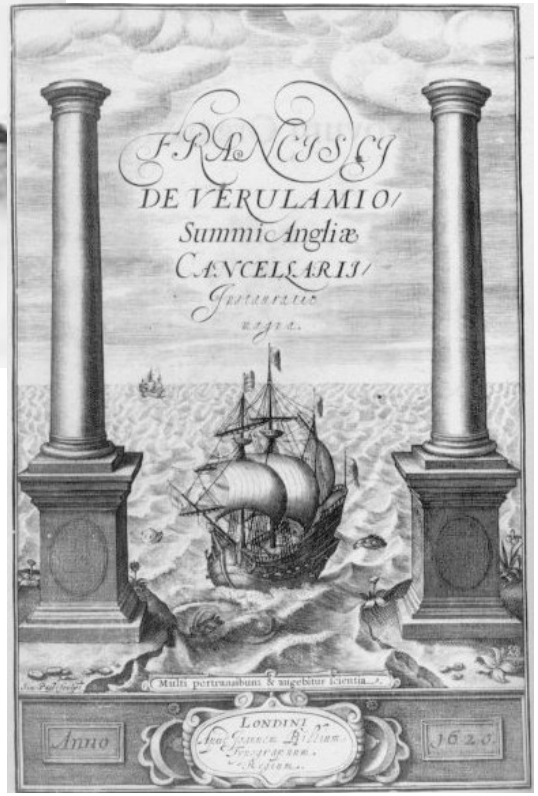
Miller, F. *NEJM* 2003; 348:1383–1386



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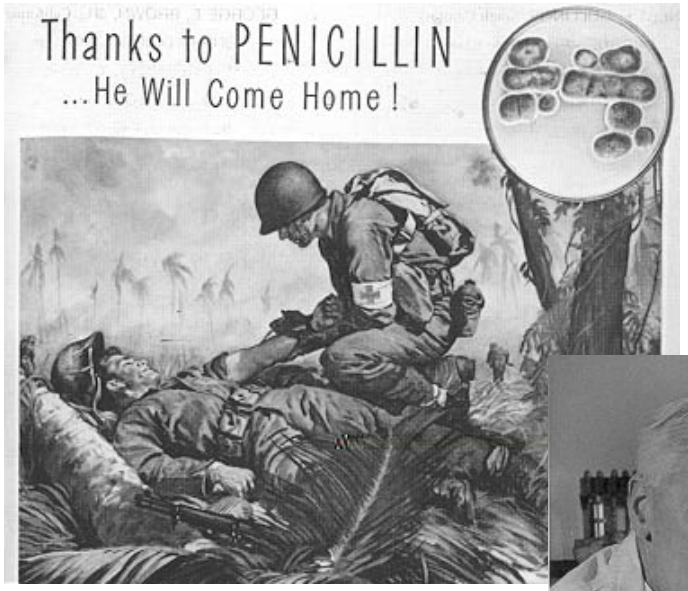

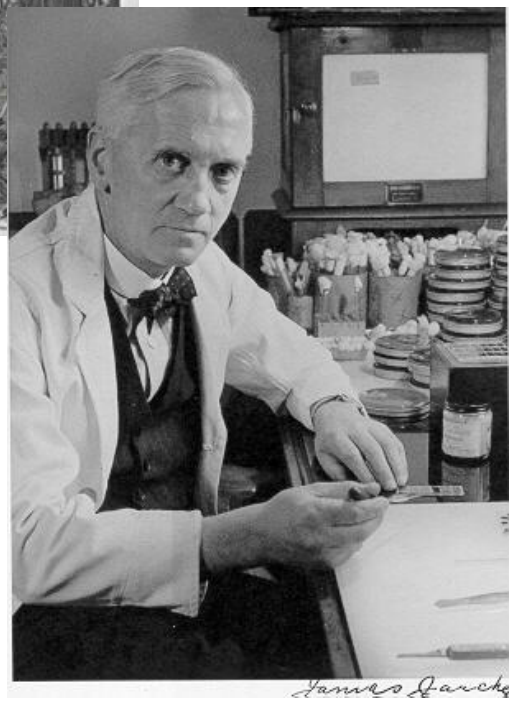

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Telford Taylor (1908-1998)

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☞ Código de Nüremberg

2.- El experimento debe realizarse **con la finalidad de obtener resultados fructíferos para el bien de la sociedad,** que no sean procurables mediante otros métodos o maneras de estudio, y no debe ser escogido al azar ni ser de naturaleza innecesaria.

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☞ Declaración de Helsinki

21. La investigación médica en seres humanos sólo debe realizarse cuando **la importancia de su objetivo** es mayor que el riesgo inherente y los costos para la persona que participa en la investigación

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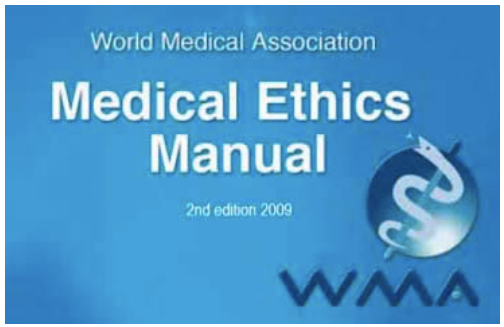
☞ **Uno de los requisitos más polémicos de un proyecto de investigación médica es que contribuya al bienestar de la sociedad en general**. Se aceptaba ampliamente que los avances en el conocimiento científico tenían un valor intrínseco y no necesitaban otra justificación.



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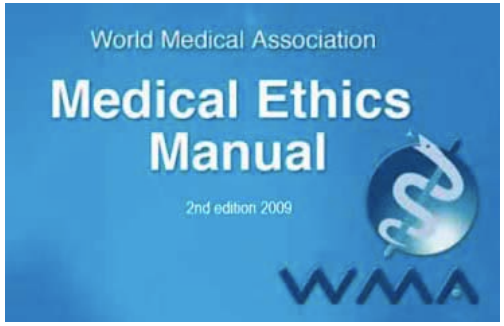
☞ Sin embargo, **puesto que los recursos disponibles para la investigación médica son cada vez más insuficien**tes, el valor social ha surgido como un criterio importante para decidir si un proyecto debe ser financiado…



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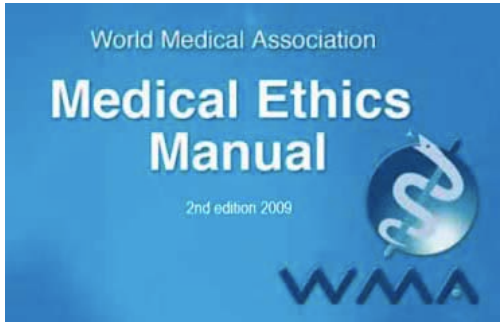
☞ El valor social de un proyecto de investigación es más difícil de determinar que su mérito científico, pero no es una buena razón para ignorarlo.

Los investigadores y los comités de revisión ética deben asegurarse que los pacientes no sean sometidos a exámenes que es probable que no tengan ningún propósito social útil.



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THE AMERICAN JOURNAL OF PSYCHIATRY

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Reviews and Overviews

Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine: An Exploratory Analysis of Head-to-Head Comparison Studies of Second-Generation Antipsychotics

Heres et al. Am J Psychiatry 2006; 163:185–194

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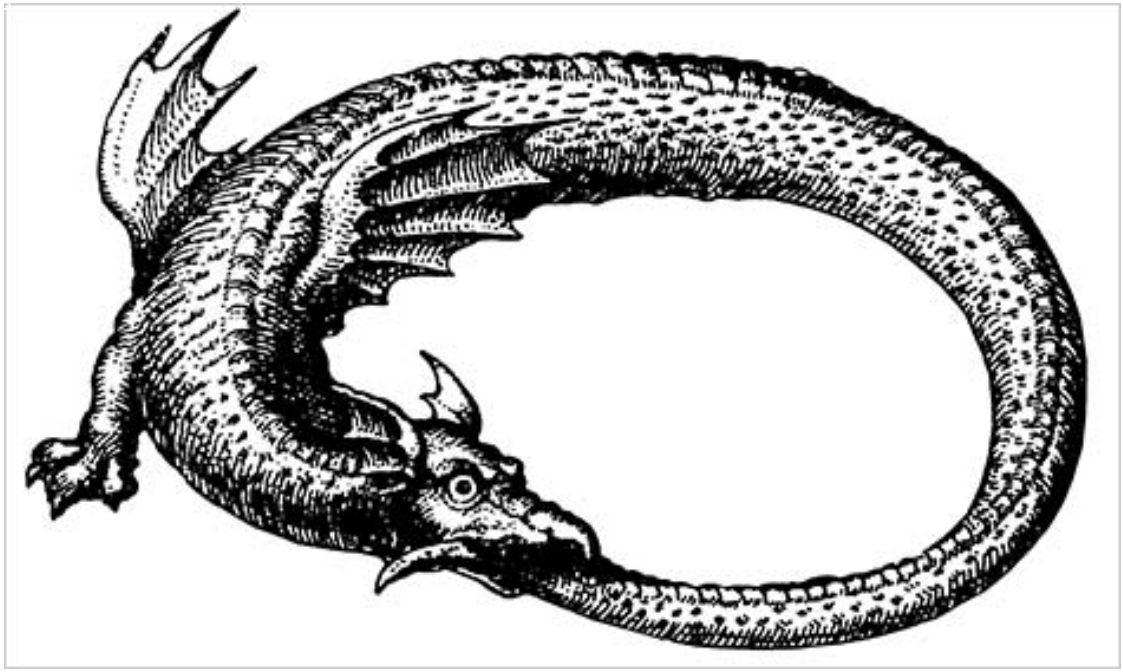

Heres et al. Am J Psychiatry 2006; 163:185–194

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Discussion

The first part of our analysis revealed a clear link between sponsorship and study outcome as reported in the abstract, as 90.0% of the abstracts were rated as showing an overall superiority of the sponsor's drug. This finding is in accordance with numerous previous reports of a similar effect in other medical fields (3, 4, 6, 69). Even more striking were our findings for pair-wise comparison of different trials that examined the effects of the same two drugs (Table 1). We found that different comparisons of the same two antipsychotic drugs led to contradictory overall conclusions, depending on the sponsor of the study. On the basis of these contrasting findings in head-to-head trials, it appears that whichever company sponsors the trial produces the better antipsychotic drug. This peculiar result led us to take a closer look at various design and reporting features. Indeed, a number of potential reasons for the association between drug-company-sponsored trials and favorable results were identified.

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Heres et al. Am J Psychiatry 2006; 163:185–194

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TABLE 1. Number of Reports That Favor the Study Sponsor's Drug or the Comparison Drug in Industry-Sponsored Head-to-Head Comparison Studies of Second-Generation Antipsychotics

Second-Generation Antipsychotic Pair and Sponsor of Study	Number of Reports Favoring Sponsor's Drug or Comparison Drug	
	Sponsor's Drug	Comparison Drug
Olanzapine versus risperidone		
Lilly	5	0
Janssen	3	1
Olanzapine versus clozapine		
Lilly	2	1
Novartis	1	0
Clozapine versus risperidone		
Novartis	1	0
Janssen	1	0
Ziprasidone versus olanzapine		
Pfizer	1	1
Lilly	2	0
Amisulpride versus olanzapine		
Lilly	1	0
Sanofi-Synthelabo	1	0

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Heres et al. Am J Psychiatry 2006; 163:185–194

☞ ¿Fraude?

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Ready T. News Feature: "The color of money".

Nature Medicine 9, 1340 - 1341 (2003)

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☞ ¿Sesgo?

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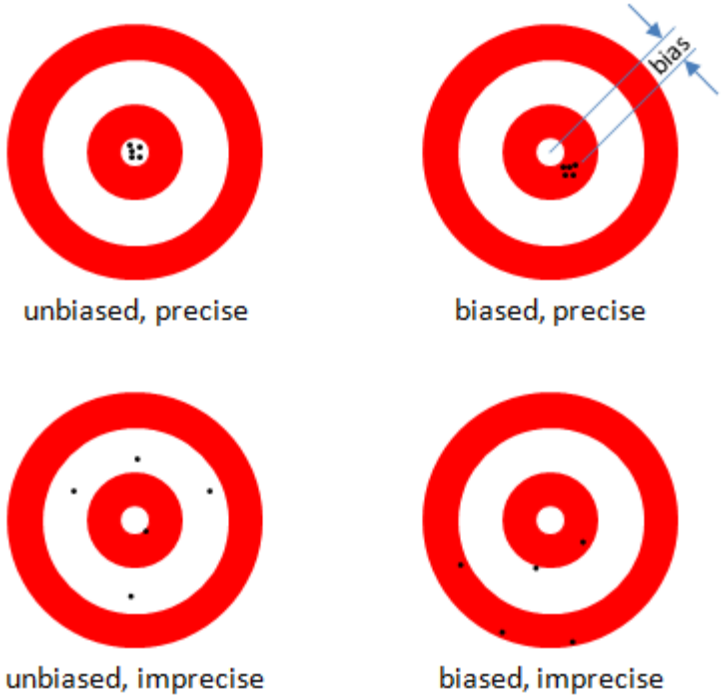

www.statisticalengineering.com/Weibull/precision-bias.html

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Posibles Fuentes de Sesgo

- Uso inadecuado de exclusiones al ingreso
- Dosis de comparación inadecuadas
- Utilización de placebo habiendo droga efectiva
- Publicación selectiva de resultados

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☞ Origen del Sesgo

- …
- Aparición de un tercer interés en conflicto.

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- **Profits 2011**
  - Lugar 17: Pfizer US$ 10.009 millones
  - Lugar 19: Johnson & Johnson US$ 9.672 millones
  - Lugar 29: Merck US$ 6.272 millones
  - Lugar 42: Eli Lilly US$ 4.347 millones

http://money.cnn.com/magazines/fortune/fortune500/2012/performers/companies/profits/

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- **Investigaciones con *dudoso* valor social**
  - Fármacos "yo también" (*me-too drugs*)
  - …

http://www.eulabor.org/en/index.html

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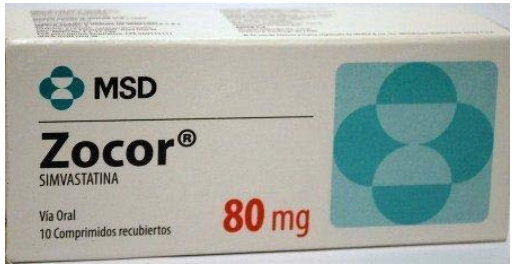

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- **Investigaciones con *dudoso* valor social**
  - Fármacos "yo también" (*me-too drugs*)
  - Intervenciones marginalmente eficaces
  - …

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 10, 2006 VOL. 355 NO. 6

High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators*

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CONCLUSIONS

In patients with recent stroke or TIA and without known coronary heart disease, 80 mg of atorvastatin per day reduced the overall incidence of strokes and of cardiovascular events, despite a small increase in the incidence of hemorrhagic stroke. (ClinicalTrials.gov number, NCT00147602.)

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Miller, F. *NEJM* 2003; 348:1383–1386

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RESULTS

The mean LDL cholesterol level during the trial was 73 mg per deciliter (1.9 mmol per liter) among patients receiving atorvastatin and 129 mg per deciliter (3.3 mmol per liter) among patients receiving placebo. During a median follow-up of 4.9 years, 265 patients (11.2 percent) receiving atorvastatin and 311 patients (13.1 percent) receiving placebo had a fatal or nonfatal stroke (5-year absolute reduction in risk, 2.2 percent; adjusted hazard ratio, 0.84; 95 percent confidence interval, 0.71 to 0.99; P=0.03; unadjusted P=0.05). The atorvastatin group had 218 ischemic strokes and 55 hemorrhagic strokes, whereas the placebo group had 274 ischemic strokes and 33 hemorrhagic strokes. The five-year absolute reduction in the risk of major cardiovascular events was 3.5 percent (hazard ratio, 0.80; 95 percent confidence interval, 0.69 to 0.92; P=0.002). The overall mortality rate was similar, with 216 deaths in the atorvastatin group and 211 deaths in the placebo group (P=0.98), as were the rates of serious adverse events. Elevated liver enzyme values were more common in patients taking atorvastatin.

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Supported by Pfizer.

Dr. Amarenco reports having received consulting fees from AstraZeneca, Novartis, Pfizer, and Sanofi-Aventis; lecture fees from Otsuka Pharmaceutical and Pfizer; and grant support from Pfizer. Dr. Bogousslavsky reports having received consulting fees from Pfizer and grant support from Pfizer. Dr. Callahan reports having received consulting fees from Sanofi, lecture fees from Bristol-Myers Squibb and Sanofi, and grant support from Pfizer. Dr. Goldstein reports having received consulting fees from Pfizer, Bayer, AstraZeneca, Bristol-Myers Squibb/Sanofi, GlaxoSmithKline, Merck Research Laboratories, Johnson & Johnson Cordis, and Organon; lecture fees from Bayer; and grant support from AGA Medical, Boehringer Ingelheim, the National Institutes of Health, Pfizer, and the Department of Veterans Affairs. Dr. Hennerici reports having received grant support from Pfizer and Servier. Dr. Rudolph is an employee of Pfizer and reports owning stock in the company. Dr. Sillesen reports having received consulting fees from Sanofi-Aventis; lecture fees from

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Health Care

The World's Most Expensive Drugs

Matthew Herper, 02.22.10, 06:00 AM EST

Drug prices are soaring into the stratosphere. Nine medicines now cost more than $200,000 per year.

In Depth: The World's Most Expensive Drugs

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- **Investigaciones con *dudoso* valor social**
  - Fármacos "yo también" (*me-too drugs*)
  - Intervenciones marginalmente eficaces
  - Drogas eficaces de costo catastrófico

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> US$ 400.000 / año

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  - Drogas eficaces de costo catastrófico
  - Ensayos "semilla"

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Annals of Internal Medicine

Seeding Trials: Just Say "No"

The public has lacked convincing documentary evidence of a long-suspected drug company practice: promoting a new drug by sponsoring a randomized trial in which participating physicians use the drug as they follow the trial protocol. This practice—a seeding trial—is marketing in the guise of science. The apparent purpose is to test a hypothesis. The true purpose is to get physicians in the habit of prescribing a new drug.

Ann Intern Med. 2008;149:279-280

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☞ Responsabilidades del investigador (entre otras)

- ✓ Velar por la integridad metodológica (en su diseño, conducción y reporte).
- ✓ Cumplir con las normativas de protección de los sujetos participantes.
- ✓ No disfrazar la investigación como atención.
- ✓ Comprometer el acceso público a los resultados.

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☞ Responsabilidad (adicional) del Comité de Ética

- ✓ Juzgar el valor social de la investigación y velar por la menor intromisión del interés pecuniario en el propósito de la investigación.

FONIS

CONICYT y el Ministerio de Salud establecieron desde el 2001 una línea de trabajo conjunta para buscar **una mejor vinculación entre la investigación y las necesidades del país.**

http://www.conicyt.cl/fonis/sobre-fonis/que-es-fonis/

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☞ ¿Un nuevo logo para FONIS?

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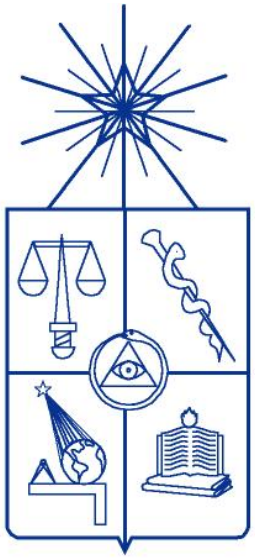

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