

Understanding and Responding to Pharmaceutical Promotion



Ventspils University College

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Health Action International

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Outline:

- Acronyms and Definitions
- Health Action International
- Interests
- Promotion Imperative
- Does Promotion Work
- How is Promotion Regulated
- Codes of Practice
- WHO Ethical Criteria
- Barriers to Effective Regulation
- Example from the Philippines (MeTA)

A Few Acronyms & Definitions.

HAI = Health Action International

WHO = World Health Organization

EML = Essential Medicines List

RUM = Responsible Use of Medicines

NGO = Non-Governmental Organisation

PINGO = Public Interest NGO

BINGO = Business Interest NGO

IFPMA = International Federation of Pharmaceutical Manufacturers Associations

EFPIA = European Federation of Pharmaceutical Industries Associations

DTCA = Direct to Consumer Advertising

TLA = Three Letter Acronym

Tying it together:

Essential Medicines

Essential medicines are those that satisfy the priority health care needs of the population ... selected with due regard to disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness

Rational Use of Medicines

Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community." (WHO, 1985).

Irrational Use of Medicines

Patients receive the wrong medications inappropriate to their clinical needs, in doses that do not meet their own individual requirements, for an inadequate period of time, and at an often unaffordable cost to them and their community.

HAI Constitution:

Article 2.1

a. to promote rational and economic medicines policy, therapy and use in high, middle and low income countries

b. to work towards global justice in health by increasing access to essential medicines and improving the rational use of medicines

Price, Availability, Affordability and Price Components

- Now over one hundred surveys, covering in excess of 2.7 billion people in low and middle income countries
- Completion of Review Series on Policies and Interventions
 - External Reference Pricing
 - Health Insurance in the Cost-Effective Use of Medicines
 - Regulation of Mark-ups
 - Competition Policy
 - Sales Taxes
 - Cost-plus Price Setting*
 - The Role of Health Technology Assessment*
- Teaching workshops (most recently Iraq)
- Monitoring Medicines Availability & Pricing (MMAP)
- *UNRWA medicine procurement prices are efficient but some improvements are needed in the procurement process (Lancet)*
- NCDs: Epilepsy. Diabetes. Cancer

* The project benefits from a grant from Iceland, Liechtenstein and Norway through the EEA Grants.

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Understanding and Responding to Pharmaceutical Promotion: A Practical Guide

- Potentially 3.5 million patients will have benefitted from the distribution of the manual
- Publication of the French edition means it is now available for download in four languages
- HAI teaching: Groningen, Vrije, Amsterdam, Latvia, Ghana
- FIP Conference stand
- PharmedOut and Selling Sickness conferences
- Peoples Health Assembly
- Won the Prix Prescrire for best new book 2013
- Now in a funding slump and WHO back-peddling

Medicines Transparency Alliance (MeTA)

- Now fully functional in seven countries: Ghana, Jordan, Kyrgyz Rep., Peru, Philippines, Uganda, Zambia
- KR: Full integration of civil society in the development of National Drug Policy - driving the process
- Jordan: Full integration of Civil Society in all expert technical committees informing JFDA policy
- Extension of civil society networks - for example CHAT and CSOs for Health
- 17 Long Haul country visits and numerous IMS visits
- IMS Management meeting later this month
- Achieved an 'A' score in DFID annual review

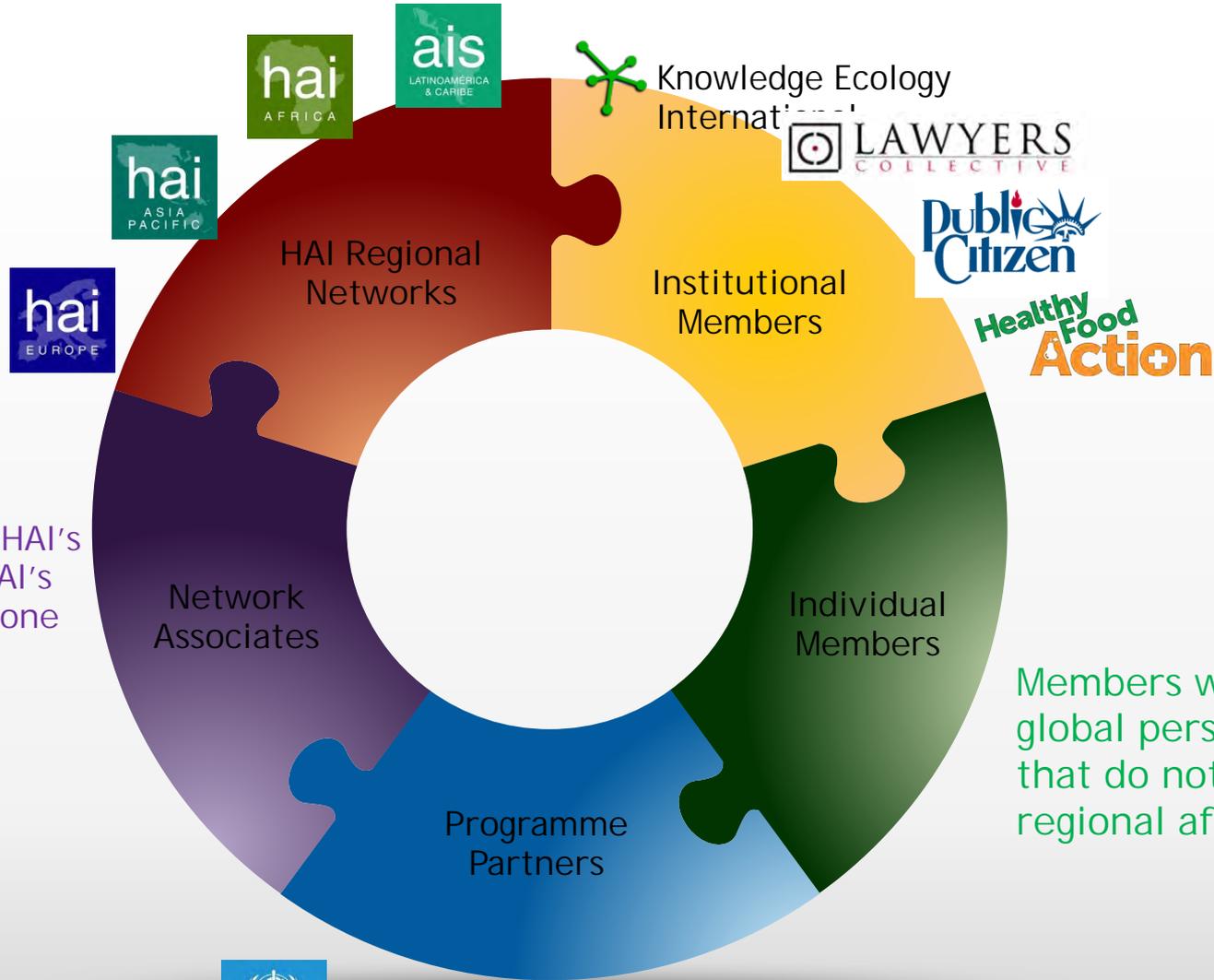
European Policy & Practice

- European Medicines Agency
- Transparency Directive (especially Clinical Trials)
- Equitable Access to Medicines in Europe
- European Policy Coherence
- Intellectual Property and Free Trade Agreements
- Secretariat for the HAI Europe Members Association

Other HAI Projects

- Actively engage in the post-MDG debate
- Actively engage in the NCD debate
- Actively engage in WHO reform debate
- Daily media monitoring/response
- Work-up proposals (currently four: EU; Dutch; insulin; AMR)
- Teach/workshops
- Anti-Microbial Resistance Coalition (ARC)
- Official Relations with WHO
- PHM Steering Committee
- Strategic Review

HAI Global Network



People who share HAI's values, work on HAI's priorities, but for one reason or another cannot be a 'card carrying' member

Members with a global perspective, that do not want a regional affiliation



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Globalisation, Interests and the Political Landscape

Pharmaceuticals Globalised Industry

- Global Space
- Free movement
- Globalisation as (the only) model of development
- Regulation of Quality, Safety, Efficacy
- Trade Agreements
- Intellectual Property
- Regulation – Intervention in an imperfect market in the public interest

All interests are affected...

Pharmaceutical Industry
Healthcare Professionals
Government
Patients
Consumers
Civil Society!

Identifying Conflict of Interest

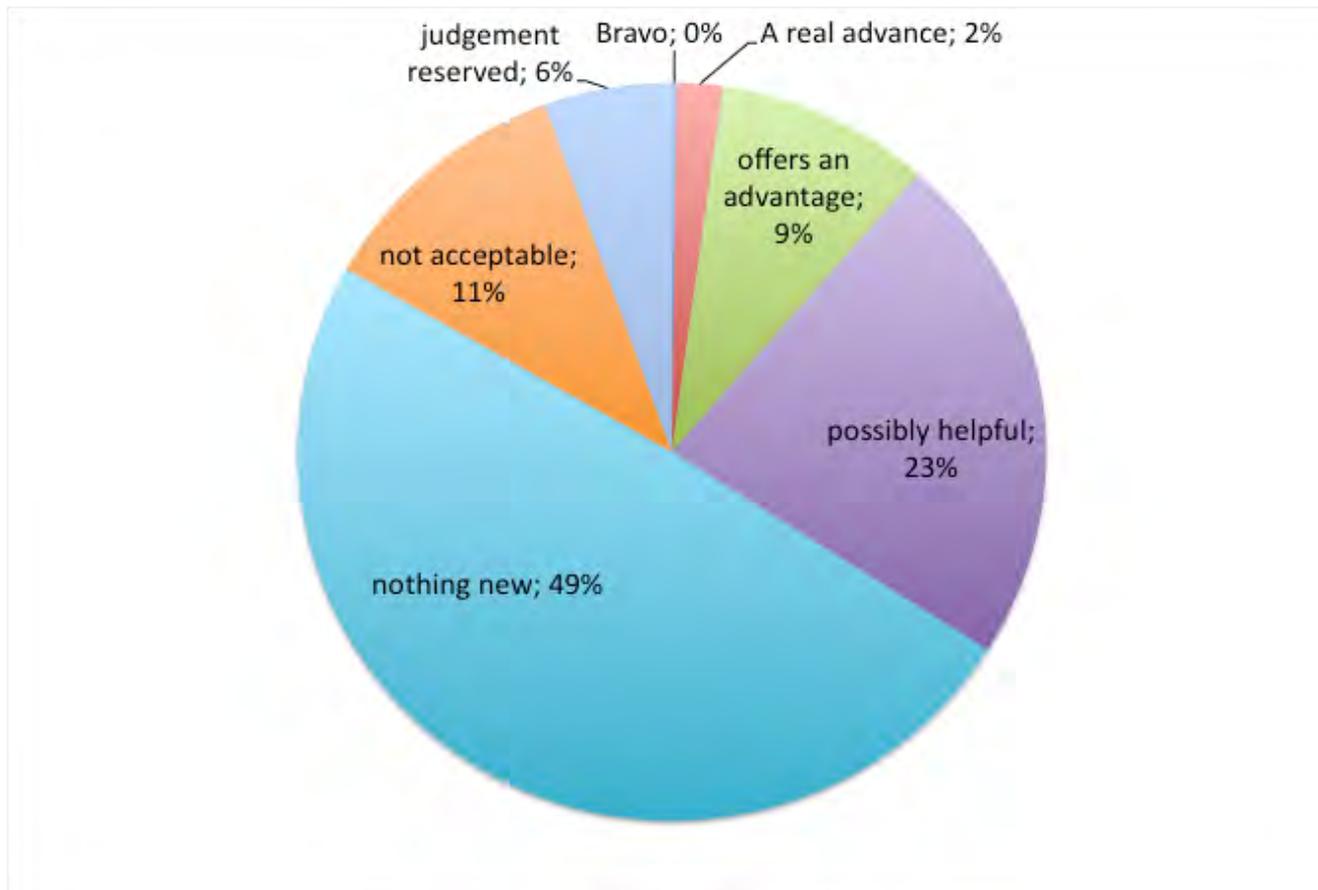
‘...an inherent conflict of interest between the legitimate business goals of manufacturers and the social, medical and economic needs of providers and the public to select and use drugs in the most rational way.’

World Health Organization, Regional Office for Europe, 1993

The Promotion Imperative

- Accountability to Share Holders = to make money
- Poor Innovation = not much therapeutic advantage
- Me-Too Medicines = more of the same
- Disease-Mongering = 'new' non-diseases
- Incentivised R&D Modelling = markets not needs

The Promotion Imperative: Innovation



Ratings of 961 new drugs and indications in France, 1999 to 2008

La Revue Prescrire

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Promotional Expenditures in Pharmaceuticals in the United States in 2004: A New Estimate

Understanding the proportions:

Sales: \$239.8 billion

R&D: \$24.1 billion (10% of revenues)

Promotion: \$57.5 billion (24.4% of revenues)

Promotion directed towards physicians: \$42.8 billion

Number of Practicing physicians: 700 000

Average promotion spending per physician: \$61,000

1 drug rep for every 6 physicians

Other undisclosed types of promotion:

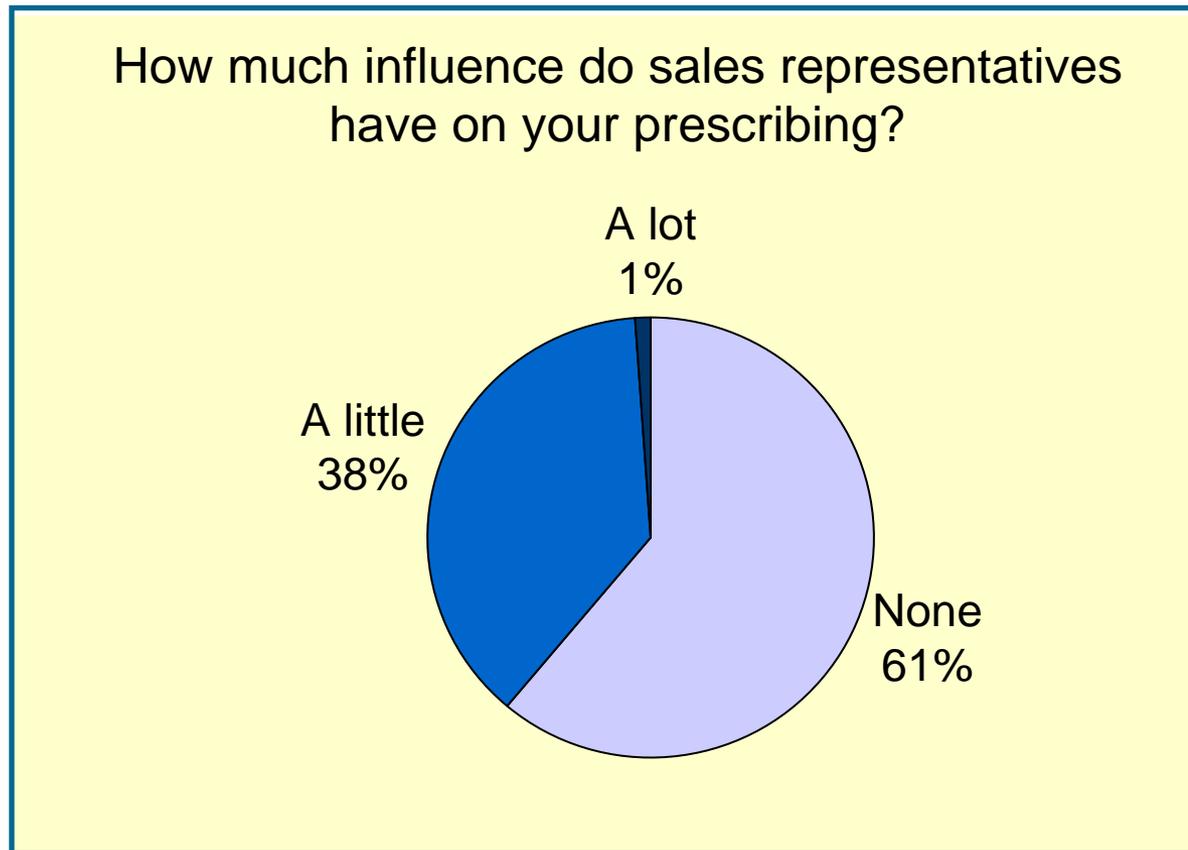
Fellowships, ghost writing, « off-label »
promotion, seeding trials



Firefox

Gagnon and Lexchin. Cost of pushing pills. PLoS Med 2008

Does pharmaceutical promotion affect prescribing: Question One

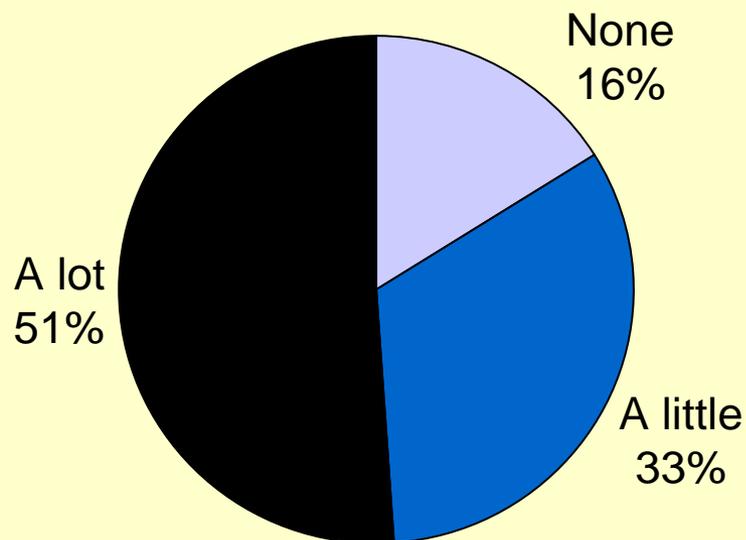


n=102 internal medicine residents

Am J Med 2001; 110:551

Does pharmaceutical promotion affect prescribing: Question Two

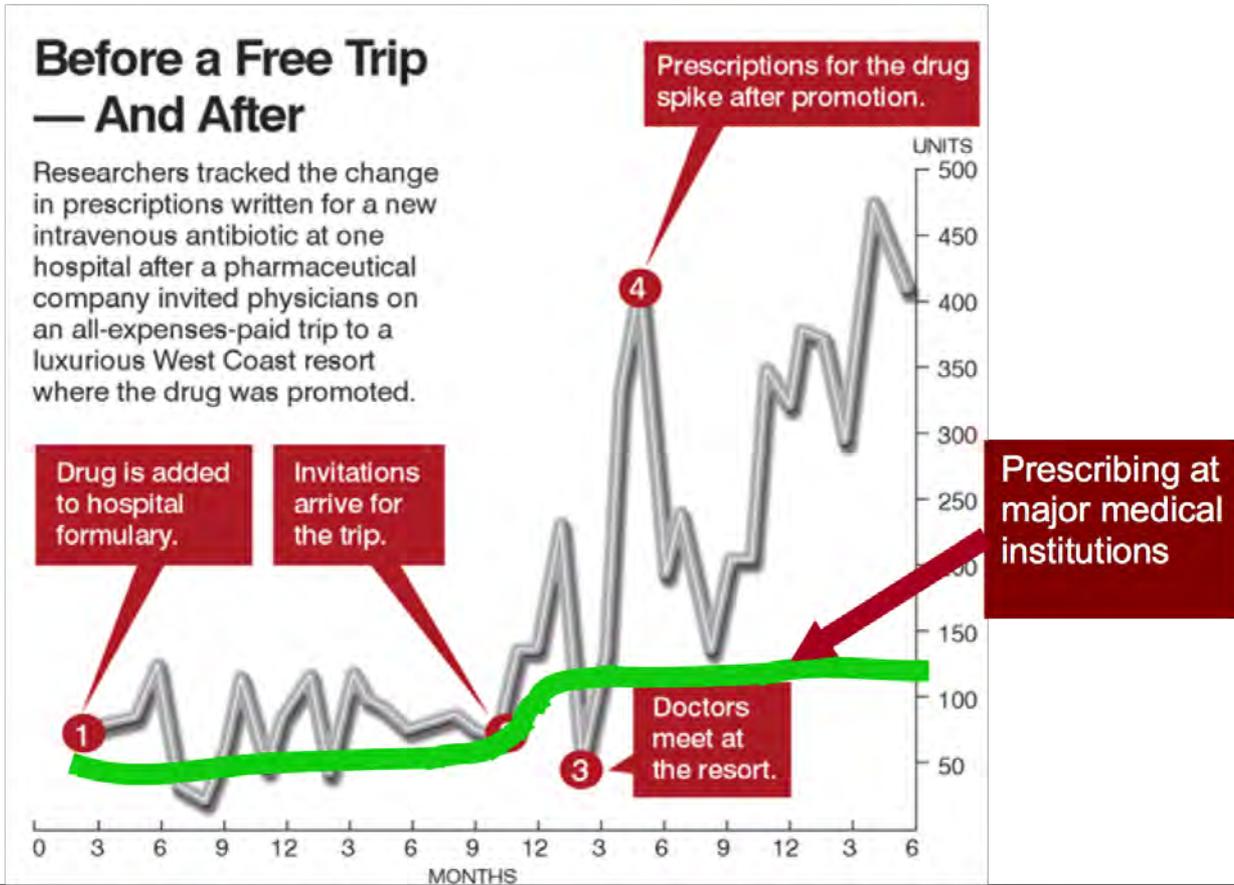
How much influence do sales representatives have on other physicians' prescribing?



n=102 internal medicine residents

Am J Med 2001; 110:551

EFFECTS OF “CME” ON VOLUME OF PRESCRIBING



Orlowski et al. Chest 1992

Widespread influence of drug promotion

In a large U.S. survey published in 2007, over 9 of 10 physicians reported some type of relationship with the pharmaceutical industry:

- 8 out of 10 received gifts, usually free food at their workplace;
- 8 out of 10 received free drug samples;
- 4 out of 10 had their expenses paid to attend meetings and conferences;
- 3 out of 10 were paid consultants, on a company speakers' bureau or advisory board

Campbell EG, Gruen RL, Mountford J et al. A national survey of physician-industry relationships.

NEJM 2007; 356: 1742-1750

Widespread influence of drug promotion

- OECD countries - physicians see an average of one sales representative a week
- Turkey (2006) >50% urban physicians in Izmir saw at least 1 sales representative each day, and 33% spent >30 minutes a day with sales reps. Although two-thirds believed that sales representatives did not influence their prescribing, most used advertisements and brochures as an information source.
- US (2005) 66% of 1640 pharmacists in hospital and community practice reported that sales representatives provide gifts that have no relation to patient care.

How is promotion regulated?

WHO World Medicines Situation: less than half of countries report that they regulate promotion (46%)

Drug promotion is a post-market regulatory responsibility

Framed by national laws

- definition of advertising - broad or limited
- normative statements: e.g. should not be deceptive, misleading, inaccurate, likely to create an erroneous impression
- may also specify information content
- prohibition of specific activities (e.g. direct-to-consumer advertising of prescription meds)

Who regulates drug promotion?

- Government regulatory authority (sometimes!)
- Often delegated to a self-regulatory body

Can be pharmaceutical industry, advertising standards or both; may be 'multi-stakeholder', also include health professions, medical media, consumers or patients

Set standards for activities and enforcement procedures

Vague Definitions

- Descriptions such as “safe” and “no side effects” should generally be avoided
- Companies must avoid using renowned or extravagant venues for events
- Hospitality provided must not exceed what participants would normally be prepared to pay
- Promotional aids of minimal value and quantity may be provided

Potential Loopholes

- National regulations usually dictate the format and content of product information on labelling, leaflets etc and in all promotional material. *Promotion should not be inconsistent with locally approved product information.*

Conflict of Interest / Absence of Effective Sanctions

- IFPMA refers complaints to an ad-hoc group of three individuals experienced in the application of national codes and selected from member associations.
- IFPMA recommends individuals from members associations for the ad-hoc groups for adjudication and appeal
- Where a breach is ruled a summary of the case will be published on the IFPMA website.

Voluntary codes for medicine promotion

- WHO Ethical Criteria for Medicinal Drug Promotion (1988)
- International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) code
- Others: World Medical Association, International Council of Nurses, International Pharmaceutical Federation, International Alliance of Patients' Organizations (IAPO)

But:

- Voluntary codes and self-regulation has limited effectiveness – no/weak sanctions
- Many generic and domestic companies are not in IFPMA
- Contemporary problem with domestic branded generics

Only mechanisms that really work:
- Strict regulation of promotional activities
- Publicly naming and shaming

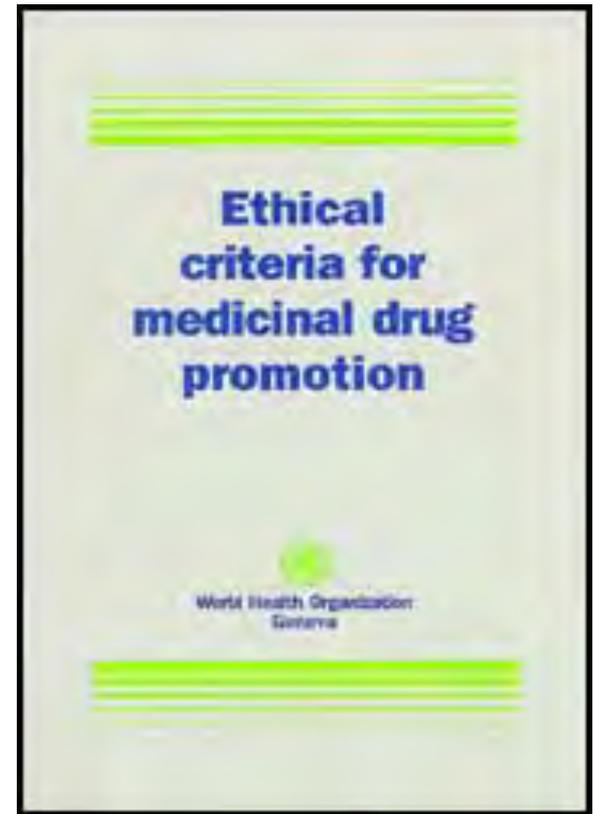
WHO Ethical Criteria

Gold Standard for codes and legislation

Never designed as a 'one size fits all'

These Criteria constitute general principles for ethical standards which could be adapted by governments to national circumstances as appropriate

....



“...claims concerning medicinal drugs should ...not contain misleading or unverifiable statements or omissions likely to induce medically unjustifiable drug use or to give rise to undue risks.”

WHO Ethical Criteria for Medicinal Drug Promotion

Omissions likely to induce medically unjustified drug use:

- most childhood acute otitis media does not require an antibiotic
- if needed, amoxicillin is the first choice.

Pediatric BIAXIN
Has Them Covered in AOM

Available in a 250 mg/5 mL Concentration

Patient To-do List
 Be a Kid

Pediatric Biaxin To-do List

- Provide Rapid Earache Relief**
 (Within 48 hours, 83% of earaches were relieved)*
- Consider Resistance**
 (Demonstrated low resistance with *H. influenzae* 1.1%, *M. catarrhalis* 2%, *S. pneumoniae* 1.6%)
- Be Kid Friendly**
 (Tastiness, no nausea, flat pants issue!)

Pediatric Biaxin is indicated for the treatment of acute otitis media caused by *H. influenzae*, *M. catarrhalis* or *S. pneumoniae*. Most commonly reported adverse events in the digestive system were diarrhea (7%), vomiting (7%), abdominal pain (2%), dyspepsia (2%) and nausea (1%).
 Biaxin XL (clarithromycin) is an antibiotic. Product Monograph available upon request.

ONCE-DAILY BIAXIN XL
 CLARITHROMYCIN EXTENDED-RELEASE TABLETS

Pediatric BIAXIN
 CLARITHROMYCIN SUSPENSION
 STRENGTH YOU CAN TRUST

*Pediatric Biaxin dosage: 15 mg/kg/day in divided doses every 12 hours, not to exceed 1000 mg/day. Pediatric Biaxin concentration: 125 mg/5 mL and 250 mg/5 mL. Pediatric Biaxin 250 mg/5 mL supplied in 105 mL unit only.
 *This study involved 2,536 individuals (aged 1 month to 16 years) with acute respiratory tract infections. Study included 32% case of otitis; 83% of patients experienced complete relief in 48 hours (total defined as mild or no symptoms).
 †Diarrhea (stool frequency) were collected in 23 medical centers in 4 practices from October 1997 to June 2002: 7,544 in *H. influenzae*, 2,314 in *M. catarrhalis* and 8,791 in *S. pneumoniae*. Child compliance has not been established.

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 www.lundbeck.com
 1 800 461-1002

For prescribing information see page 798

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sanofi aventis
Beyond Health's interests

**The First Line Treatment for "Everyday"
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全新一類Ketolide呼吸道感染的首選藥物

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衛署核字第003379號
詳細處方資料備索

Advertisement from Taiwan promotes unnecessary antibiotic use. Problematic for society (resistance) and individual patients (unnecessary exposure to potentially fatal risks).

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Brazil 2004

Boehringer Ingelheim advertisement for dipyrone drops:
“Ping-ping against pain – No Ping-ping in your purse”



We observed that, regardless of the studied medication, the information about restrictions of use, such as adverse drug reactions, interactions, contraindications, warnings and precautions, does not appear very often, and when it does, its print sizes were smaller than that of the information favoring the use.

- *Mastroianni et al, Rev Bras Psyciat 2003 (on psychoactive drug ads)*

- US study: 126 of 438 advertisements with medical claims (29%) contained references
- Of those with references 19% cited data on file (20% of these were available on request)
- Published studies much more likely to be company sponsored than articles in the same journal

Cooper and Shriver CMAJ 2005; 172:487-491

Sales representatives 15 year survey in France:

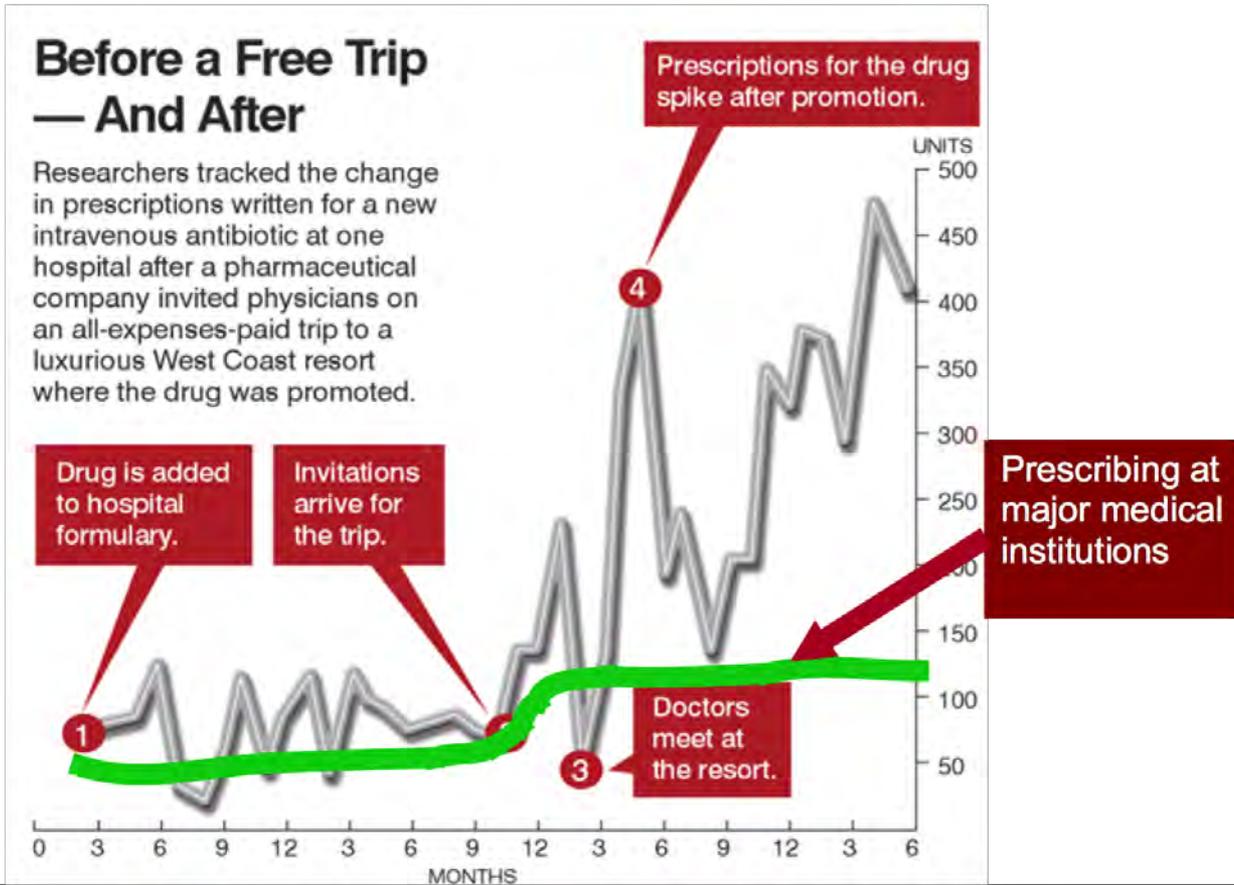
- Drug risks mentioned in 30% of promotions
- At least one unapproved indication mentioned in 25%

La Revue Prescrire, 2006

‘Promotional material should not be designed so as to disguise its real nature.’

WHO Ethical Criteria for Medicinal Drug Promotion

EFFECTS OF “CME” ON VOLUME OF PRESCRIBING



Orlowski et al. Chest 1992

Promotion using ‘opinion leaders’ Vioxx (rofecoxib)

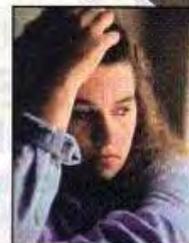
Physicians who attended sponsored presentations by another physician wrote an additional \$624 worth of prescriptions in the next year versus non-attendees. Sales visits only led to \$127/physician/year.



Caplovitz A. NJPIRG Law & Policy Center, 2006. www.njpirg.org

Frequently Asked Questions

Not Just the Teenage Blues: Adolescent Depression and Suicidality



1. What are the signs of depression?

Signs of depression include feeling "down" or agitated, decreased concentration, insomnia (initial or terminal), change in energy level, feeling fatigued, change in appetite and weight, feeling suicidal, poor self-esteem, and anhedonia.

2. What are the co-morbid conditions?

- Anxiety disorder
- Conduct disorder
- Family dysfunction
- Attention deficit hyperactivity disorder
- Learning disorder
- Neurologic conditions

For an in-depth article on adolescent depression and suicidality, please go to page 90.

As presented at McGill University

Brian Greenfield, MD, FRCP, ABPN

3. What are the genetic risk factors?

- Current or past parental depression,
- History of depression in previous generations,
- Family stress as a mediator of genetic factors.

4. What are the biological factors?

Biological factors associated with pediatric depression include positive response to fluoxetine, reduced levels of 5-hydroxytryptamine, reduced suppression of the dexamethasone suppression test, and magnetic resonance imaging and electroencephalogram findings.

Cross-sectional survey of 192 authors of 44 chronic disease clinical practice guidelines

- 59% of authors had financial relationship with manufacturers of drugs covered by the guideline
- 42/44 guidelines – no declarations of conflicts of interest

Choudry et al. JAMA 2002; 287:612-617

Do financial links matter?

- Eight of the nine authors of the US cholesterol treatment guidelines released in 2004 had financial links to statin manufacturers
- These guidelines extend treatment to patient groups in which a morbidity and mortality advantage has not been established
- From a previous 13 million, now 40 million Americans are defined as needing treatment

“While they should take account of people’s legitimate desire for information regarding their health, they should not take undue advantage of people’s concern for their health.”

- WHO Ethical Criteria for Medicinal Drug Promotion



Dire qu'un simple dosage de son **cholestérol** aurait pu lui éviter ça

Une crise cardiaque peut intervenir alors que l'on ne se croyait pas malade. On peut alors découvrir que l'on a, peut-être depuis des années, un excès de cholestérol dans le sang!

Saviez-vous qu'un excès de cholestérol peut provoquer des maladies cardiovasculaires? Et qu'elles sont la première cause de mortalité en France?

Faire doser régulièrement son taux de cholestérol est important, d'autant qu'il est relativement facile, aujourd'hui, de le faire baisser.

Des solutions existent, demandez conseil à votre médecin.

Si un seul de ces points* vous concerne, il est temps de faire doser votre taux de cholestérol.

- Homme de plus de 45 ans
- Femme de plus de 55 ans ou ménopausée
- Antécédent familial de maladie cardiaque
- Tabagisme
- Diabète
- Hypertension
- Obésité

* Agence Nationale d'Accréditation et d'Évaluation en Santé (ANAES)
Rapport d'activité 2000: Médailles de diagnostic et diagnostics biologiques des dyslipidémies en prévention primaire.

POUR PLUS D'INFORMATIONS, CONTACTEZ LE :
N°Azur 0 810 741 741



LA VIE, VOUS Y CONSACREZ NOTRE VIE

...“the information used contained misleading statements and omissions likely to cause medically unjustifiable drug use or to give rise to undue risks.”
-Quick et al. *Lancet* Aug 30, 2003

prevention-**cardio**.com



Canada 2005



Peru 2006

Same drug, same company, same promotional campaign

- Unapproved use
- Illegal direct-to-consumer advertising
- Costly and not very effective

I am Julie

Last vacation was the first time I ever dared to wear a bikini!

What would you do with a few pounds less?

I tried and tried to lose weight on my own for so long. Then a friend at work told me there are medical weight loss treatments available, and said I should go and see my doctor. I'm glad I did — my doctor was fantastic. If you want to start losing weight, you should ask your own doctor.

Ask your doctor about Julie's story.

MEDICAL TREATMENT OPTIONS AVAILABLE

* The project benefits from a grant from Iceland, Liechtenstein and Norway through the EEA Grants.

Public advertisement, Guatemala 2006 & 2010



"Tengo **diabetes**,
si mi medicamento falla
podría sufrir **un coma diabético**."

YO NO ME LA JUEGO
uso sólo **ORIGINALES**.

Los medicamentos originales
cuentan con estudios que respaldan su calidad, eficacia y seguridad



Respete la receta médica. Pregunte a su médico o regente farmacéutico cuál es el medicamento original.



"I have diabetes. If my medication fails, I could suffer a diabetic coma"

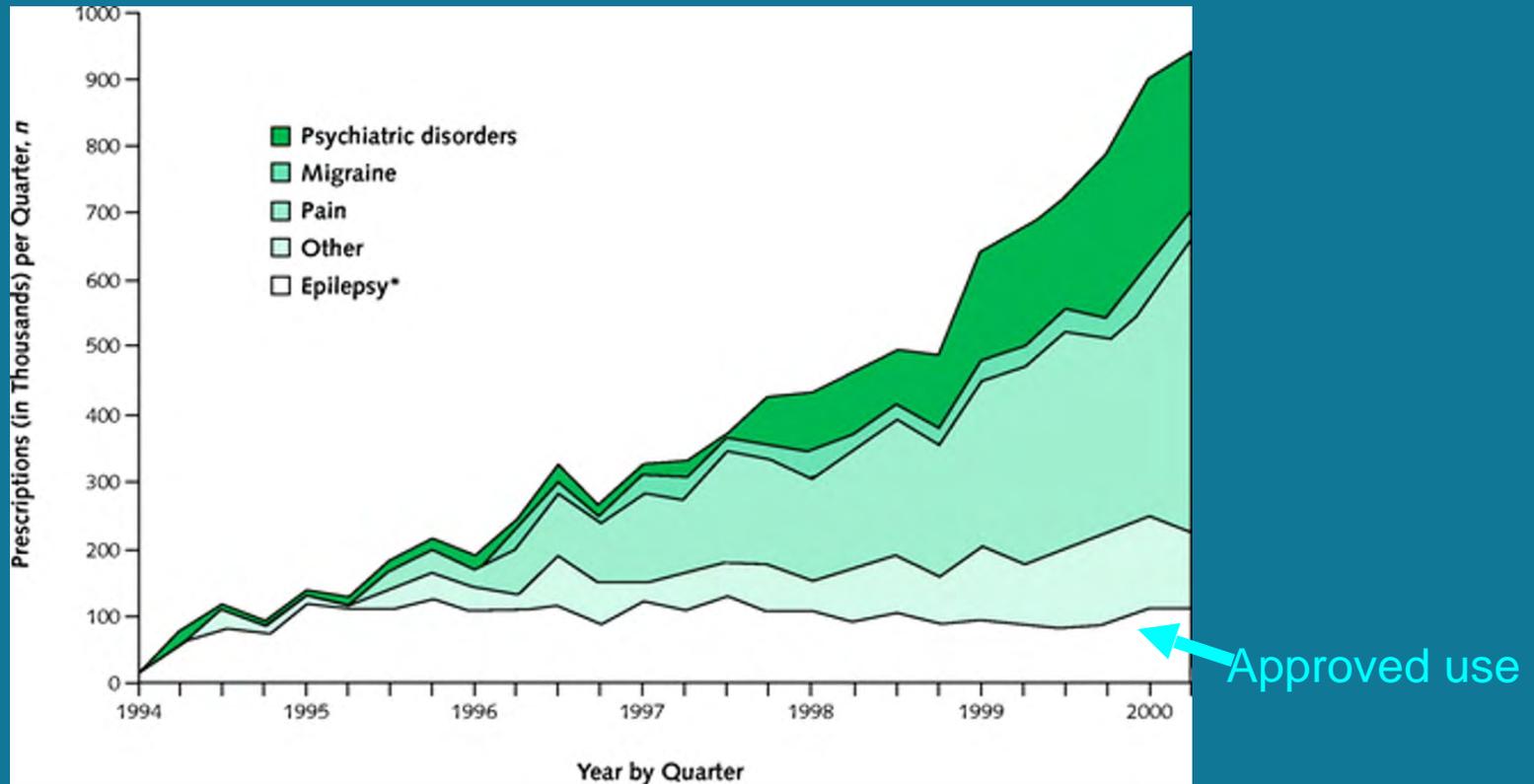
"I don't take chances. I only use original"

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“Scientific and educational activities should not be deliberately used for promotional purposes.”

WHO Ethical Criteria for Medicinal Drug Promotion

“Gabapentin [Neurontin] was promoted by using education and research, activities not typically recognized as promotional. “independent” continuing medical education, “peer-to-peer” selling by physician speakers, and publications...”



Prescriptions for gabapentin by diagnostic category

Steinman, M. A. et. al. Ann Intern Med 2006;145:284-293

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“Promotion in the form of financial or material benefits should not be offered to or sought by health care practitioners to influence them in the prescription of drugs.”

- WHO Ethical Criteria for Medicinal Drug Promotion

Oct 2005, Vancouver, Canada:

Bayer invites “15 local pain specialist practitioners with knowledge and expertise in treating multiple sclerosis” to participate in the “Sativex Pain Specialist Regional Advisory Board”, taking place in Vancouver, Dec 6, 2005 (4:30 – 7:30 pm), Hyatt Regency

“In appreciation of your participation and feedback, we are pleased to extend an honorarium of \$1,250... Dinner will be provided following the program.”

“[advertising to the public] should not generally be permitted for prescription drugs...”

WHO Ethical Criteria for Medicinal Drug Promotion



Burnaby General Hospital (suburb of Vancouver) March 2006
 Celecoxib is not on the hospital formulary and direct-to-consumer
 advertising is illegal in Canada

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Barriers to effective regulation

- weak standards
- no active monitoring
- non-transparent complaints procedures
- no correction of misinformation
- burden of proof on complainant, ads run during adjudication
- sanctions ineffective, “the price of doing business”
- no systematic evaluation of effectiveness
- published evaluations and exposés of promotion that distorts science (academic, NGO, courts) have had little effect on regulatory procedure
- the sheer volume of promotional activity
- Poor resources and capacity of DRA

What could be the components of a national framework to promote good governance and prevent corruption?

Ethical framework of moral values & ethical principles

- Justice/fairness
- Truth
- Service to common good

Code of conduct



- Established anti-corruption legislation
- Whistle-blowing mechanism
- Sanctions on reprehensible acts
- Transparent and accountable regulations and administrative procedures

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Countering unethical promotion

Advocate for:

- Establishment of a rational use unit in the DRA or MoH
- Appropriate legislation and sanctions, effective implementation and full enforcement
- Training of medical and other health professional students (both before and after graduation)
- Provision of reliable non-commercial therapeutic information to professionals and the public
- Monitoring medicines promotion

Possible corruption by doctors

- Receiving medical representatives, wasting time on biased info when you are ill-prepared
- Accepting gifts from pharmaceutical companies (pens, taxis, free meals, conferences, partners, etc)
- Accepting samples “to test the product yourself”
- Accepting donations of medicines which are not in the formulary
- Participating in promotional trials, receiving cash or computer
- Dispensing doctor, prescribing medicine with highest profit or accepting cash discounts on drugs to be sold
- Financial kick-back based on number of prescriptions
- Participating in formulary committees while also receiving research contracts or speakers’ honorarium from manufacturers

Mexico Principles



Open to interpretation

All Events should be held in an **appropriate** venue that is conducive to the scientific or educational objectives and the purpose of the Event or meeting. Companies should **avoid using extravagant** venues or resorts.

Nothing should be offered or provided by a Company in a manner that **inappropriately influences** a healthcare professional's prescribing practices.

Biggest problem is voluntary code!

A Model for Discussion

Based on oversight of self regulation

Primary Legislation: for example a Drug Promotions (Ethical Criteria) Act to

1. Define the meaning of Drug Promotion
 2. Outline the penalties for infringement
 3. Appoint agencies below
- A. Office of Oversight: DRA or MOH
1. Uphold requirements of the Act
 2. Monitor performance of Designated Authority
 3. Set fees and fines
- B. Designated Authority: for example Pharmaceutical Manufacturers Association
1. Monitoring, detection, investigation
 2. Responsibility to report to Office of Oversight
 3. Implement regulation
- C. Audit and Appeals Committee: multi-stakeholder
1. Independent, with substantial lay representation
 2. Commitment to public health, recognition of interests and truth
 3. Receive, note and refer complaints
 4. Hear appeals

Paying for it

Central Taxation:

Public good that improves
public health and saves money!

Fees paid by pharmaceutical industry:

Part of approval process
Approval of strategy
Linked to promotion spend

Fees to users:

Sales tax

Fines:

Large enough to hurt!

Further Information

www.haiglobal.org

links to other sites in the network, European campaigns, promotions manual, methodology for measuring promotion enforcement, MeTA, Price and Availability methodology and interactive maps

www.politicsofmedicines.org

Unique encyclopaedia of the politics of medicine, accessible essays that will grow and change with time