Le modèle d'affaires de la pharmacie:
Des profits fondés sur le contrôle du savoir médical

Présentation pour le

Collège des Médecins du Québec

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PLAN DE LA PRÉSENTATION

Section 1: Portrait de l'économie politique du secteur pharmaceutique

Section 2: Portrait global de la promotion pharmaceutique

Section 3: Impact de la promotion sur la pratique médicale, la formation et la recherche en médecine

Section 1:

Portrait de l'économie politique du secteur pharmaceutique

Quelques indicateurs

- En 2008, le marché global des médicaments représentait environ US$750 milliards, soit 3,3% de la production industrielle mondiale.
- De 2000 à 2008, le PIB mondial a augmenté en moyenne de 4,1% par année, alors que les ventes de médicaments ont augmenté de 8,7% par année.
- Au Québec, en 1985 les médicaments représentaient 8,3% des dépenses de santé alors qu'en 2008 ils représentaient 20,7%. La croissance des coûts en médicaments est responsable de plus du quart de la croissance des coûts en santé.

Fusions Acquisitions

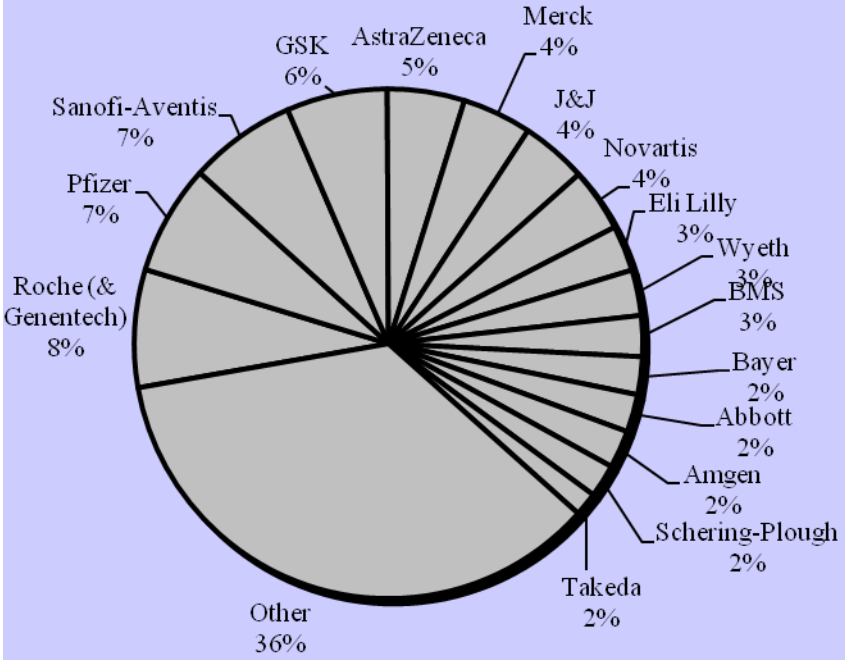
List of Big Pharma Companies, Sept. 30 2008

Company	Country	FT Global 500 Rank	Market Value (Billion $)
1- Johnson and Johnson	US	10	193.6
2- Novartis	Switzerland	25	138
3- Roche	Switzerland	26	134.3
4- Pfizer	US	31	124.3
5- GlaxoSmithKline	UK	38	112.6
6- Genentech	US	53	93.6
7- Abbott Laboratories	US	58	88.8
8- Sanofi-Aventis	France	59	86
9- Merck	US	77	67.6
10- AstraZeneca	UK	83	63.5
11- Amgen	US	85	62.7
12- Bayer	Germany	106	55.6
13- Eli Lilly	US	111	50.1
14- Wyeth	US	115	49.3
15- Bristol-Myers-Squibb	US	150	41.3
16- Takeda Pharmaceutical	Japan	155	40.3
17- Schering Plough	US	220	30
Total	-	-	**1431.6**

Source: FT Global 500, Fortune Global 500

Big Pharma = 64% des ventes mondiales

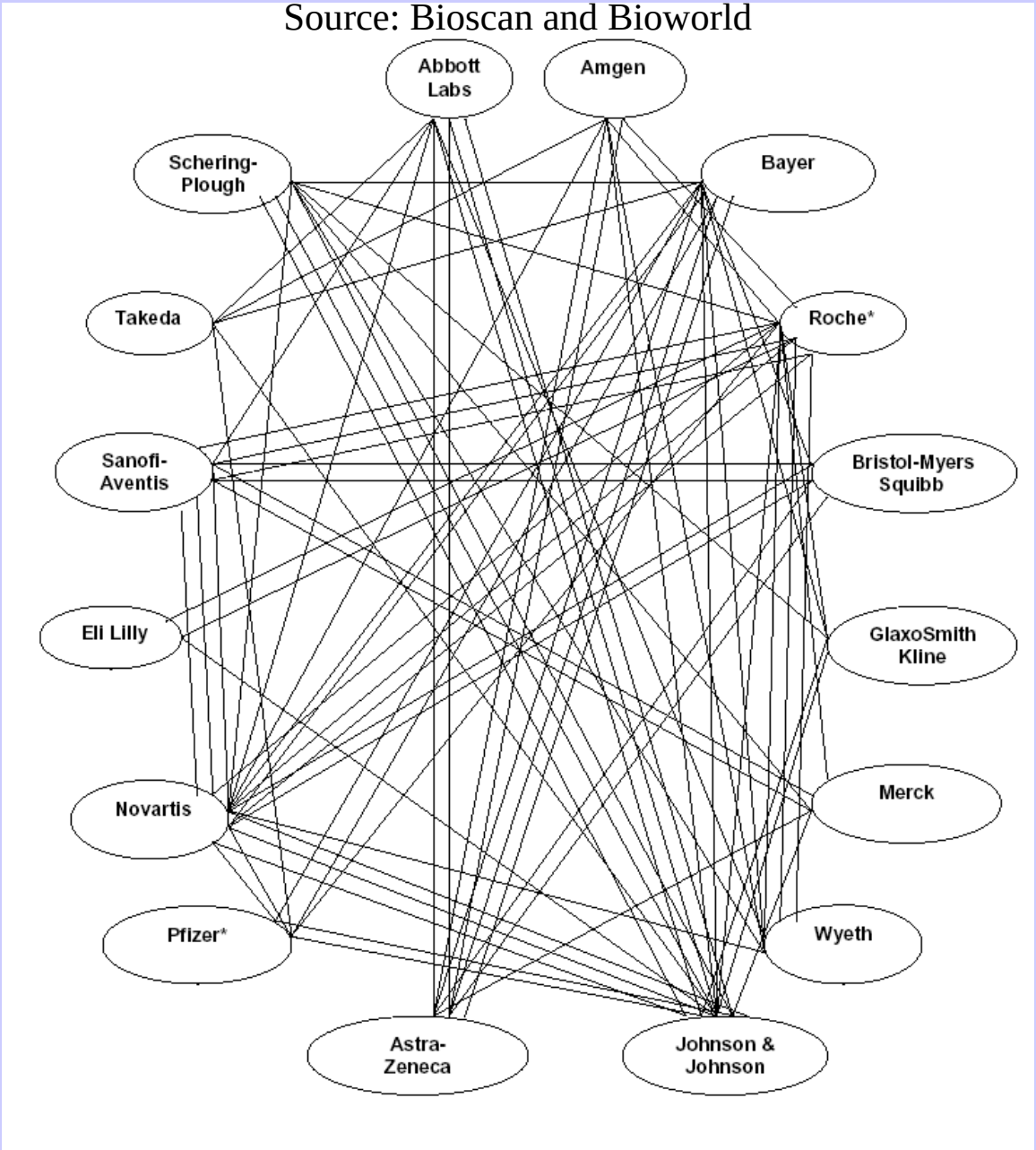
Drug Sales as a Share of Total Market, 2007



Sources: Cowen and Co. (Investext), Takeda and Bayer corporate websites

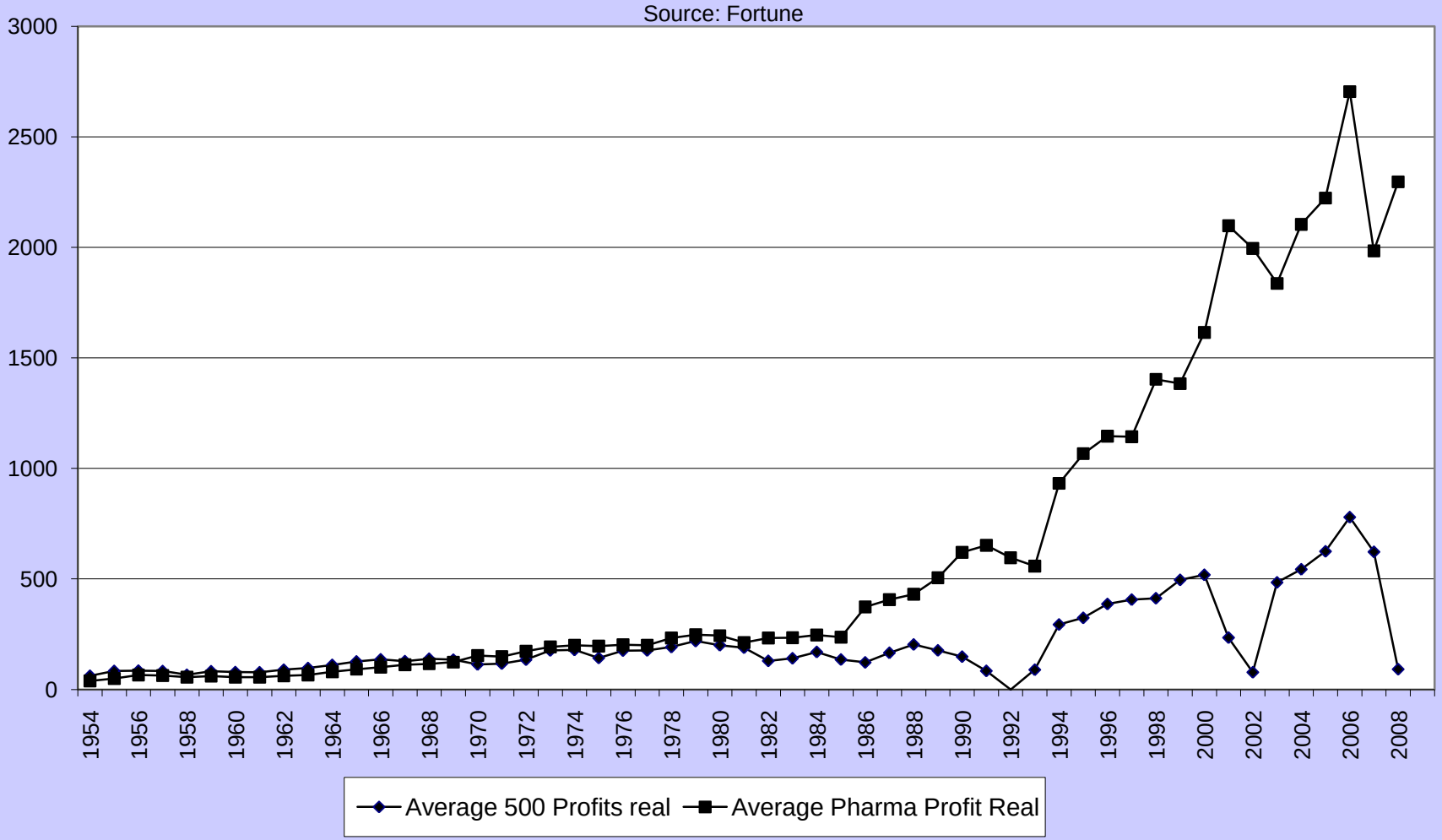
On-Going Cooperation Agreements Among Big Pharma, May 2008

Source: Bioscan and Bioworld



Accumulation Différentielle de Big Pharma;

Profits d'une firme pharmaceutique américaine dominante moyenne par rapport à ceux d'une firme dans le Fortune 500
(1954-2008; en millions de US$ constants de 1984) (2 mai 2009)

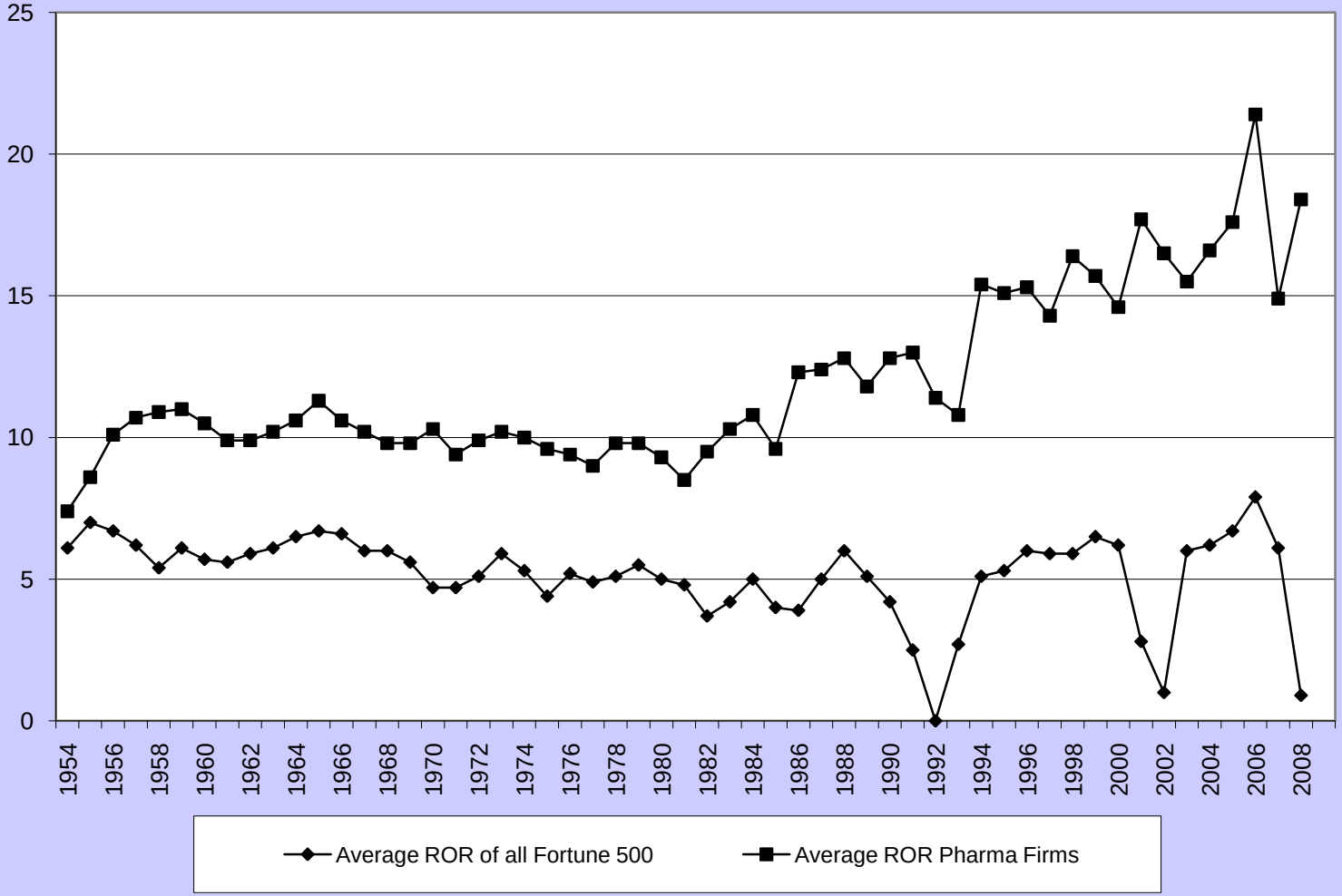


Évolution différentielle du taux de profits

(Profits par unité de médicaments)

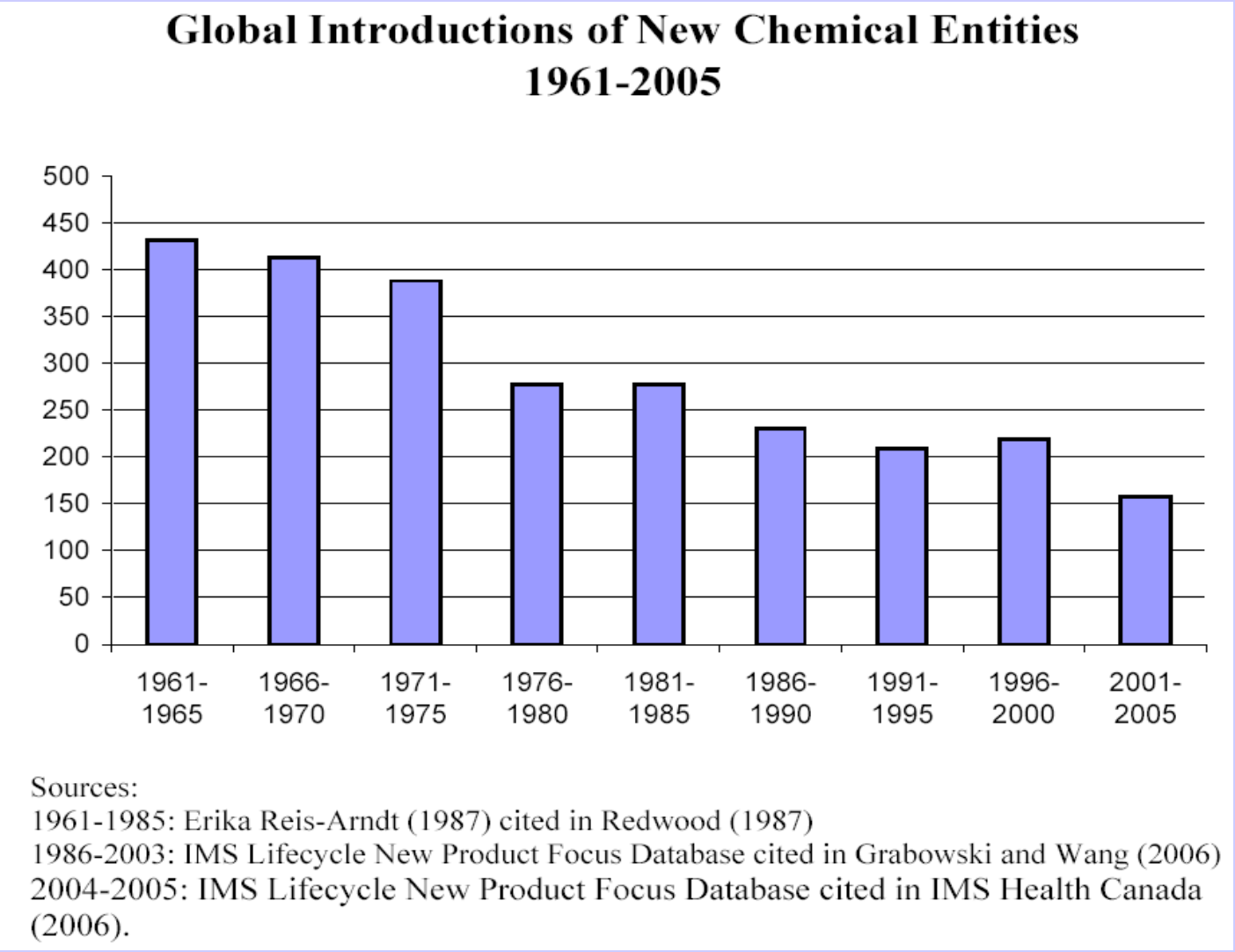
1954-2008

Source: Fortune Magazine (Updated May 2, 2009)



Entrons-nous dans une nouvelle ère de l'innovation?

Analyse quantitative

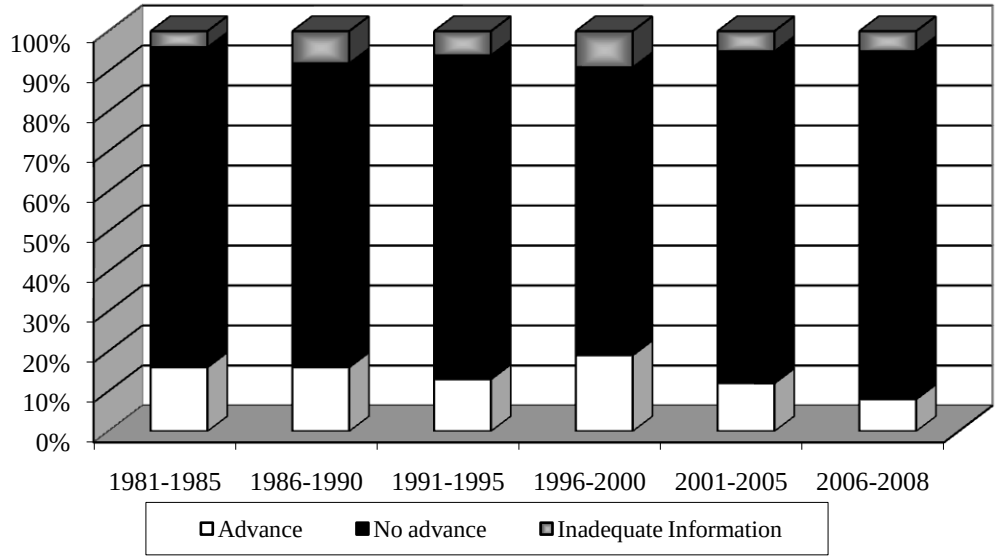


Sources:
1961-1985: Erika Reis-Arndt (1987) cited in Redwood (1987)
1986-2003: IMS Lifecycle New Product Focus Database cited in Grabowski and Wang (2006)
2004-2005: IMS Lifecycle New Product Focus Database cited in IMS Health Canada (2006).

Entrons-nous dans une nouvelle ère de l'innovation?

Analyse qualitative

Percentage of New Drugs Representing a Therapeutic Advance in the French Pharmacopoeia, 1981-2008



Sources: Prescrire (#213 p.59; #224 p.56, #280 p.142; #304 p.139).

- En 2008, 120 nouveaux médicaments ont été introduits en France.
-6 représentaient des avancées thérapeutiques
- 105 n'apportaient rien de nouveau
- 23 ont été sévèrement critiqués par les médecins qui y voyaient un danger réel pour la santé.

Section 2:

Portrait global de la promotion pharmaceutique

Quel impact de la promotion pharmaceutique?

- **En théorie:**
  - **↑ Promotion = ↑ Unités vendues**
  - **↑ Coût total de production mais**
  - **↓ Coût moyen par unité, donc**
  - **↓ des prix**

Quel impact de la promotion pharmaceutique?

- **En pratique: « Charge what the traffic will bear! »**

  – **Avastin:** Médicament anticancer (bevacizumab). 20-60$ dose mensuelle. Usage off-label efficace pour la dégénérescence maculaire liée à l'âge (DMA). Genentech, le fabricant, s'est opposé à ce que les autorités autorisent ce médicament pour traiter la DMA et a plutôt produit un dérivé sous le nom de Lucentis (ranibizumab), coût de production moyen plus bas que pour Avastin mais permet d'allonger les brevets. 2000$ la dose mensuelle. (http://www.patentdocs.net/patent_docs/2007/10/genentech-acts-.html)

  –**Sarafem:** Lorsque le brevet de Prozac est arrivé à échéance, le fabricant, Eli Lilly, a développé une nouvelle niche pour le produit grâce à une grande campagne promotionnelle (PMS or PMDD). Même pilule, même dosage mais couleur différente (rose et lavande plutôt que bleu). Prix trois fois plus élevé que Prozac (lorsque protégé par brevet).

Promotion et Prix des médicaments

Un médecin est un acheteur sans contrainte budgétaire. Souvent, il ne connaît même pas le prix des produits qu'il prescrit.

Demande sans contrainte

=

El Dorado de la science économique

Dépenses en promotion pharmaceutique aux États-Unis en 2004:

Marc-André Gagnon et Joel Lexchin, "The Cost of Pushing Pills: A New Estimate of Pharmaceutical Promotion Expenditures in the United States", *PLoS Medicine*, vol. 5, #1, Janvier 2008: pp.1-6.

Table 7.3: A New Estimate: Pharmaceutical Promotional Spending in the United States in 2004

Type of Promotion	Billion $	% of Total
Retail Value of Samples (IMS)	15.9	27.7%
Sales Rep Contacts (CAM)	20.4	35.5%
DTCA (CMR)	4	7%
Meetings (CAM)	2	3.5%
E-Promotion, mailing, clinical trials (CAM)	0.3	0.5%
Journal Advertising (IMS and CAM)	0.5	0.9%
Undisclosed marketing (CAM)	14.4	25%
Total	**57.5**	**100%**

Source: IMS, CAM, CMR

Dépenses en promotion pharmaceutique aux États-Unis en 2004: Nouvelle estimation

<u>Chiffres ajustés selon données des médecins</u>:

Ventes: 239.8 Md$

R&D: 24,1 Md$ (10% des ventes)

Promotion: 57.5 Md$ (24,4% des ventes)

Promotion auprès des médecins: 42.8 Md$

Nombre de médecins actifs: 700 000

1 représentant pharmaceutique pour 6 médecins

Promotion par médecin: 61 000$

Autres formes promotionnelles non répertoriées:
Bourses, ghost writing, promotion « off-label »,
Essais cliniques de phase IV

La promotion a le vent dans les voiles

De 1996 à 2004, aux États-Unis:

-Le nombre de médecins a augmenté de 38%.

-Le nombre de représentants pharmaceutiques a augmenté de 150%.

-Le nombre de meetings promotionnels a augmenté de 254%.

-Les médecins 10% Top prescribers ont reçu de 2 à 4 fois plus de visites de représentants.

-Le financement privé de l'éducation médicale continue a augmenté de 465%, dépassant le financement public pour ce type d'éducation.

- La publicité dirigée vers les patients a augmenté de 509%.

État de la situation:

1-Modèle d'affaires basé sur les me-too drugs.

2-Baisse d'innovation thérapeutique mais croissance des profits car contrôle sur les structures du savoir médical continue de s'accroître. (Demande sans contrainte budgétaire)

3- Deux fois plus de dépenses en promotion qu'en R&D.

Section 3:

Impact de la promotion sur la pratique médicale, la formation et la recherche en médecine

Leaders d'opinion: Construire le discours médical en fonction des ventes

Les leaders d'opinion sont des médecins reconnus payés par l'industrie (~3000$) pour animer des meetings éducationnels ou informatifs (environ 2/3 des meetings)

Kimberly Elliott, manager de représentants pharmaceutiques:

"KOL were salespeople for us, and we would routinely measure the return on our investment, by tracking prescriptions before and after their presentations. If that speaker didn't make the impact the company was looking for, then you wouldn't invite them back" (quoted in Moynihan 2008, 1402).

Comment mesure-t-on le retour sur l'investissement? IMS Health offre le profil de prescription de chaque médecin et son évolution dans le temps.

Physician Category	Technique	How It Sells Drugs	Comments
Friendly and outgoing	I frame everything as a gesture of friendship. I give them free samples not because it's my job, but because I like them so much. I provide office lunches because visiting them is such a pleasant relief from all the other docs. My drugs rarely get mentioned by me during our dinners.	Just being friends with most of my docs seemed to have some natural basic effect on their prescribing habits. When the time is ripe, I lean on my "friendship" to leverage more patients to my drugs...say, because it'll help me meet quota or it will impress my manager, or it's crucial for my career.	Outgoing, friendly physicians are every rep's favorite because cultivating friendship is a mutual aim. While this may be genuine behavior on the doctor's side, it is usually calculated on the part of the rep.
Aloof and skeptical	I visit the office with journal articles that specifically counter the doctor's perceptions of the shortcoming of my drug. Armed with the articles and having hopefully scheduled a 20 minute appointment (so the doc can't escape), I play dumb and have the doc explain to me the significance of my article.	The only thing that remains is for me to be just aggressive enough to ask the doc to try my drug in situations that wouldn't have been considered before, based on the physician's own explanation.	Humility is a common approach to physicians who pride themselves on practicing evidence-based medicine. These docs are tough to persuade but not impossible. Typically, attempts at geniality are only marginally effective.
Mercenary	The best mercenary docs are typically found further down the prescribing power scale. There are plenty of 6's, 7's, and 8's [lower prescribing doctors] who are eagerly mercenary but simply don't have the attention they desire fawned on them. I pick a handful out and make them feel special enough with an eye towards the projected demand on my limited resources in mind. Basically, the common motif to docs whom you want to "buy out" is to closely associate your resource expenditure with an expectation—e.g., "So, doc, you'll choose Drug X for the next 5 patients who are depressed and with low energy? Oh, and don't forget dinner at Nobu next month. I'd love to meet your wife."	This is the closest drug-repping comes to a commercial exchange. Delivering such closely associated messages crudely would be deemed insulting for most docs so a rep really has to feel comfortable about their mercenary nature and have a natural tone when making such suggestions.	Drug reps usually feel more camaraderie with competing reps than they do with their clients. Thus, when a doctor fails to fulfill their end of the prescriptions-for-dinners bargain, news gets aroun and other reps are less likely to invest resources in them.
High-prescribers	I rely on making a strong personal connection to those docs, something to make me stand out from the crowd.	Friendship sells. The highest prescribers (9's and 10's) are every reps sugar mommies and daddies. It's the equivalent of spitting in the ocean to try to buy these docs out because, chances are, every other rep is falling head over heels to do so.	The highest prescribers receive better presents. Some reps said their 10's might receive unrestricte "educational" grants so loosely restricted that they were the equivalent of a cash gift, although I did not personally provide any grants.
Prefers a competing drug	The first thing I want to understand is why they're using another drug as opposed to mine. If it's a question of attention, then I commit myself to lavishing them with it until they're bought. If they are convinced that the competitor drug works better in some patient populations, I frame my drug to either capture another market niche or, if I feel my drug would fare well in a comparison, I hammer its superiority over the competing drug.	If, during the course of conversations, the doctors say something that may contradict their limited usage of our products, then the reps will badger them to justify that contradiction. This quickly transforms the rep from a welcomed reprieve to a nuisance, which can be useful in limited circumstances. We force the doctors to constantly explain their prescribing rationale, which is tiresome. Our intent is to engage in discourse but also to wear down the doc until he or she simply agrees to try the product for specific instances (we almost always argue for a specific patient profile for our drugs).	For reps this is a core function of our job. We're trained to do this in as benign a way as possible. No doc likes to be told their judgment is wrong so the latter method typically requires some discretion.
Acquiescent docs	Most docs think that if they simply agree with what the rep says, they'll outsmart the rep by avoiding any conflict or commitment, getting the samples and gifts they want, and finishing the encounter quickly. Nothing could be further from the truth. The old adage is true, especially in pharmaceutical sales: there is no such thing as a free lunch.	From the outset of my training, I've been taught to frame every conversation to ultimately derive commitments from my clients. With every acquiescent nod to statements of my drug's superiority I build the case for them to increase their usage of my product. They may offer me false promises but I'll know when they're lying: the prescribing data is sufficiently detailed in my computer to confirm their behavior. Doctors who fail to honor their commitments, no matter how casually made, convert the rep into a badgering nuisance. The docs are often corralled into a conversational corner where they have to justify their previous acquiescence.	Gifts are used to enhance guilt and social pressure. Reps know that gifts create a subconscious obligation to reciprocate. New reps who doubt this phenomenon need only see their doctors' prescribing data trending upwards to be convinced. Of course, most of these doctors think themselves immune to such influence. This is an illusion reps try to maintain.
No-see/ No-time (hard-to-see docs)	Occasionally docs refuse to see reps. Some do it for ethical reasons, but most simply lack the time. Even when I don't manage to see the doctor, I can still make a successful call by detailing the staff. Although they're on the doc's side for the most part, it's amazing how much trouble one can rile up when the staff are lavished with food and gifts during a credible sounding presentation and then asked to discuss the usage of a drug on their patients.	It's a victory for me just to learn from the staff about which drugs are preferred, and why. That info provides powerful ammunition to debate the docs with on the rare occasions that I might see them. However, it's a greater success when the staff discusses my meds with the doc after I leave. Because while a message delivered by a rep gets discounted, a detail delivered by a co-worker slips undetected and unfiltered under the guise of a conversation. And the response is usually better then what I might accomplish.	One's marketing success in a particular office can be strongly correlated to one's success in providing good food for the staff. Goodwill from the staff provides me with critical information, access, and an advocate for me and my drug when I'm not there.
Thought leaders	As a rep, I was always in pursuit of friendly "thought leaders" to groom for the speaking circuit. Once selected, a physician would give lectures around the district. I would carefully watch for tell-tale signs of their allegiance. This includes how they handled questions that criticized our product, how their prescribing habits fluctuated, or simply how eager they were to give their next lecture.	The main target of these gatherings is the speaker, whose appreciation may be reflected in increased prescribing of a company's products. Local speaking gigs are also auditions. Speakers with charisma, credentials, and an aura of integrity were elevated to the national circuit and, occasionally, given satellite telecast programs that offered CMEs.	Subtle and tactful spokespersons were the ideal candidates. I politely dismissed doctors who would play cheerleader for any drug…at the right price, of course.

These descriptions are based on SA's experience working for Eli Lilly and testimony in IMS Heath Inc. v. Ayotte, US District Court, New Hampshire. Actual tactics may vary.

doi:10.1371/journal.pmed.0040150.t001

Représentants pharmaceutiques: Adapter sa relation et les techniques de vente selon la personnalité du médecin.

Fugh-Berman A, Ahari S (2007) Following the Script: How Drug Reps Make Friends and Influence Doctors. PLoS Med 4(4): e150 April 24 2007.

Les jeux d'influence de Big Pharma dans la recherche médicale

-Lorsque "niche" putative apparait: déplacement du financement de la recherche. (Bourses, Prix).

- 70% de financement externe de R&D de l'industrie à Contract Research Organizations (Firmes de relations publiques), 30% à université avec entente de non-divulgation.

-Ghost writing de masse critique d'articles dans les revues médicales (sertraline (Zoloft): 85 manuscrits/211 titres, 479 keywords)

-Australasian Journal of Joints and Bones Medicine (+ 18 autres revues par Merck)

-Non-divulgation des études défavorables:

Cas des anti-dépresseurs:74 essais cliniques sur nouvelle génération (38 pour, 36 contre)
36 favorables publiées, 8 défavorables publiés (dont 5 comme si résultats positifs)

Zetia/Vytorin (avec Zocor): Depuis 2006, essais cliniques montraient clairement que les médicaments n'apportaient aucun bénéfice pour réduire risques d'attaques cardiaques. 1 Million de prescriptions par semaine jusqu'au début 2008 (2 milliards de vente).

- Cherry-Picking des résultats et des leaders d'opinion; Production du discours plus important que médicaments.

Essais cliniques de phase IV (postmarketing)

• 13,2% du budget de recherche et développement consacré aux essais de phases IV.

• 75% de ces essais n'existent que pour des fins promotionnelles (seeding trials).

• Le but est de mobiliser le médecin, lui faire croire qu'il participe à une étude, à faire avancer la connaissance

•Étude sur de grandes populations. Médecins payés de 100 à 500$ par patients.

-34 033 Canadiens enrôlés sur Diovantage (Diovan, Novartis), pour analyser leur compliance, (Que doit faire Merck avec son Cozaar pour concurrencer Diovan?)

- 4500 Patients dans régions de Québec et Montréal pour Obstat (Pfizer et Astra-Zeneca) qui vise à analyser la compliance pour statines chez les nouveaux patients.

•Pourtant, le manque de bons essais de phase IV (ou non-diffusion des résultats) empêche d'évaluer la dangerosité de certains médicaments sur de larges populations.

Impacts sur les habitudes de prescriptions

Exemple des anti-hypertenseurs:

-Étude de ALLHAT (2002) montraient que la nouvelle génération des anti-hypertenseurs (Angiotensin-Converting Enzyme Inhibitor ou Calcium Channel Blocker), prescrits systématiquement par les médecins, étaient en fait moins efficaces que l'ancienne génération (diurétiques) qui coûtaient 10 fois moins chers.

-Les habitudes de prescription ont-elles changé depuis? Pas du tout, les firmes ont enrôlé une série de leaders d'opinion pour attaquer systématiquement les résultats de l'étude et pour « noyer le poisson » (Pollack 2008).

Même constat pour les antipsychotiques (Jones et al. 2006).

Antidépresseurs? (Healy 2008; Jureidini 2009; Spielmans 2009).

Les “nouvelles tendances” promotionnelles

- Budget croissant pour leaders d’opinion et formation continue.
- Programmes de support à l’observance pour les Blockbusters (CV Success Zone). [Voir Critique par l’IGAS 2007; Biron et al. 2009].
- Empowerment du patient par Publicité directe [Canwest, Celebrex, Gardasil].
- Création de Revues Médicales à des fins promotionelles: Merck et l’Australasian Journal of Joints and Bones Medicine (+ 18 autres revues)
- Organisation des stratégies publicitaires autour des usages Off-Label (Neurontin et Zyprexa).[Voir Steinman et al. 2006; Spielmans 2009]
- Emphase sur les marchés émergents puisque davantage de possibilité pour firmes pour “former” les médecins.

Le principal problème

Même le médecin le plus compétent n'est plus assuré de pouvoir obtenir des informations neutres et objectives lui permettant de prescrire les produits les plus efficaces pour ses patients. La promotion pharmaceutique s'étant immiscée dans l'ensemble de la pratique médicale, le médecin est amené à prescrire des produits au rendement thérapeutique douteux, mais offrant un meilleur rendement financier pour l'entreprise.

La promotion n'est pas au service du patient ou de la santé publique, elle est au service de l'entreprise. Et elle fait mourir à petits feux la recherche pharmaceutique et l'éthique médicale…

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