



# NEWSLETTER

Vol. 15, N°3, October 2001

**AN ISDB MEMBER FROM SPAIN  
(BASQUE PROVINCES) HAS  
CHANGED ITS NAME**

*Información Farmacoterapéutica de la Comarca (Infac)* is the new name of this monthly bulletin. The old one was *Informacion Farmacoterapéutica Vasca*.

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## COLUMN

### About the word consumer

This newsletter carries several papers about direct-to-consumer advertising. The word 'consumers', used instead of 'patients', is used increasingly in medical publications. In reality a consumer is: 'A person who purchases goods and services for his own needs' (Collin's dictionary). The word 'consumer' therefore is more than a euphemism and a soothing word for 'patient'. Indeed using the term tends to negate the role of doctors and pharmacists and patient-professional relationship. The term consumer assumes the patient is independently and reliably informed, and can choose from the medicines on offer to treat any health problems: this is not common practice.

The word 'consumer' also has commercial connotations. It puts implicit and sometimes inappropriate emphasis on the role of drug

treatments, and tend to overlook non-drug options (surgery, therapeutic abstention, psychotherapy, etc.). Those with vested interests may therefore prefer the term consumer since it is consistent with the concept of direct-to-consumer advertising, e-commerce of medicines, and the industrial strategy of bypassing health professionals who are viewed as barriers to expanding drug markets.

Making the patients and the public informed and committed partners in health care is a desirable aim. But the word *consumer* should be avoided when describing the relation between patients and medicines. The word 'consumers' should be replaced by 'the public' or the 'patients'. Occasionally the word 'individuals' may be appropriate since those taking medicines to prevent some events (e.g. pregnancy or malaria) are not 'patients'.

## Contents

### COLUMN

About the word consumer..... p. 1

### THE REGULATORY WATCHDOG

Direct-to-consumer advertising by default in Canada ..... p. 2  
Direct-to-consumer advertising: two Canadian organisations report ..... p. 3  
Direct-to-consumer advertising in the European Union? ..... p. 3  
Direct advertising of prescription drugs on the agenda in Europe ..... p. 4  
The novelty factor..... p. 4  
EU centralised procedure does not mean a drug is innovative ..... p. 5  
Some drug agencies are more open than

others ..... p. 6  
Direct-to-consumer advertising: the New Zealand situation..... p. 6

### NEWS OF BULLETINS

*La revue Prescrire's* Reps Monitoring Network ..... p. 8  
*Therapeutic Guidelines Limited* and the Australian Pharmaceutical Benefits Scheme..... p. 9  
*InfoPharma* Israel Prescribing Guide 2001 ..... p. 10  
*Arznei-telegramm* on pseudo-innovative drugs ..... p. 11

### EDITORIAL METHODS

The second CONSORT statement.... p. 13

### GOOD SOURCES

Two reference sources on drug regulation in Europe ..... p. 13  
*E-drug* electronic conference..... p. 13  
*No Free Lunch* ..... p. 15  
The October 2000 Declaration of Helsinki..... p. 16  
*Public Citizen Congress Watch* and industry's R&D myths..... p. 21

## DTCA IN CANADA

*Despite the law, Canada is on the verge of de-facto Direct-to-consumer advertising*

Pierre Trudeau, a former Canadian Prime Minister once told an American audience that “living next to you is like sleeping with an elephant; no matter how friendly and even-tempered is the beast, one is affected by every twitch and grunt.”

It was an apt description of Canada’s position relative to the United States, and could be easily applied to a whole variety of Americanizing influences shaping health and social policy in Canada.

The differences in health care systems in Canada and the US are profound, and are particularly noticeable in the contrasting sets of laws governing direct-to-consumer advertising (DTCA).

As most people are well aware, in the United States, prescription drug manufacturers are relatively unhampered by controls on commercial free speech and hence we have seen spending on DTCA grow enormously over the last decade. Last year companies in the US spent over \$2 billion advertising its drugs to consumers, a rapid acceleration of growth since 1997 when the US relaxed its advertising rules. Spending on DTCA currently accounts for approximately 20% of drug companies’ promotion budgets, and there is every indication that competition through DTCA is likely to become more intense in the future.

Because we sleep next door to an elephant, Canadians have been flooded with DTCA via US television, radio and magazines. Technically, drug companies in Canada are not permitted to directly market their products to consumers, but there is evidence that the growth of DTCA in the US since the 1990’s, has found the Canadian government playing a very passive role in enforcing the ban on it in Canada.

In fact, a number of proponents of DTCA in Canada point to the drug advertising we pick up on US airwaves and websites and say, “look, it’s already here”. But drug companies here at home are adding to the cacophony of drug messages flowing unimpeded across our long border. A number of drugs such as Alesse, Zyban and Propecia

have been advertised directly to the public in Canada’s largest cities despite the ban. Having a complaint-driven enforcement system in Canada means that it is only after citizens (or rival drug firms) complain to the federal government that anything is done. And violations usually kick off lengthy investigation processes that may take several months to complete. Just long enough for the ad campaign to have had its effect.

Critics of the lax enforcement of Canada’s anti-DTCA laws, such as Barbara Mintzes who is heading a government-funded DTCA study in Vancouver, maintain that the government has all but stopped enforcing the prohibition, making de-facto DTCA a reality in Canada.

It is true that the way the Canadian ban has been interpreted seems to allow grey areas in our law to be easily exploitable by some drug companies who wish to push the law’s boundaries. The government has been known to sometimes side with the companies, claiming certain kinds of consumer drug ads are actually legal—these include reminder ads and “help-seeking” ads. An ongoing overhaul of Canada’s national health protection legislation is underway, and it will determine what kind of DTCA will be allowed in the future. It is still too early to tell but there is an indication that the government is considering its political options before opening the doors even further to more DTCA.

Other critics of DTCA in Canada include groups as the *Canadian Medical Association*, the *Canadian Pharmacists Association*, the *Consumer’s Association of Canada*, several provincial governments and other health groups. They have been vocal in opposing the move to legalise DTCA in Canada. There has even been some international input into the Canadian campaign to stop DTCA before the gates are opened.

Peter Mansfield of *Healthy Skepticism* in New Zealand came to Canada in May to do a cross Canada tour and talk about the risks of DTCA. As an expert in the marketing of pharmaceuticals, he has studied first hand what he calls the ‘devastating effects’ of DTCA in countries such as New Zealand and the United States.

His trip to Canada, sponsored by a coalition of women’s health groups and funded by *Health Action International*, met with key policy makers and health organisations in most of Canada’s major cities—Vancouver, Victoria, Winnipeg, Toronto, Ottawa and Montreal.

The polarized environment Dr. Mansfield saw in Canada during his stay, was characterized by, on one side, a number of the provincial governments fiercely opposed to DTCA because of fears that it would drive up drug benefit plan costs.

On the other side was evidence that multinational drug companies, advertising agencies and media interests were lobbying government in the hopes of profiting from relaxed Canadian laws and expanded DTCA.

Mansfield noted that the current level of unenforced violations of the law has seen “companies pushing to see what they can get away with before their competition beats them to it.”

Canada’s next move on DTCA is still undecided. Some experts say there is draft legislation on the books that only needs to be approved by the government. How long that will take is anyone’s guess. One way or another, it seems the Canadian government is waiting for the right political climate before they’ll allow new legislation in this area to ever see the light of day.

Certainly what is happening in Europe is extremely worrying. Joel Lexchin, a pharmaceutical industry analyst from Toronto worries that if other countries move closer to legalising DTCA, it would further weaken “what little resolve there is left in Health Canada to keep DTCA out of the country.”

*Alan Cassels (drug policy researcher, Canada)*

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## DTCA IN CANADA

### *Two Canadian organisations report*

#### **DES Action Canada**

The United States and New Zealand are the only countries where it is legal to advertise prescription drugs to consumers. Drug company lobbyists are pushing hard for law amendments to that effect in other regions, Europe for instance.

Direct-to-consumer advertising of prescription drugs (DTCA) is prohibited in Canada, yet Health Canada (the official body) is not adequately enforcing the law, as reported by *DES Action Canada* with the Canadian *Working Group on Women and Health Protection* in two excellent booklets. One booklet is titled: "Direct-to Consumer Prescription Drug Advertising: When Public Health is No longer a Priority". Looking at

the Canadian situation the authors show why it is so important to prohibit DTCA of prescription drugs, and to oppose its legalisation.

The other booklet is titled: "Illegal direct-to consumer prescription drug advertising in Canada, 1999 to 2001- When drug companies skirt the law and the government refuses to enforce, who pays?"

The booklet are available free to ISDB members upon request at: [desact@web.net](mailto:desact@web.net)

We also recommend you to visit *DES Action Canada's* web site: [www.web.net/~desact](http://www.web.net/~desact)

#### **Therapeutics Initiative**

In its *Therapeutics Letter* n° 40, this Canadian ISDB member explores a typical case of DTCA for a prescription drug (finasteride for male hair loss), and tells us how to man-

age the situation:

"Mr. Jones (26 years old) comes in to see you about a cough he has had for 3-4 weeks. You've just finished listening to his chest and reassured him that it's the aftermath of a viral infection. He asks you, "By the way, I'm wondering about this pill I saw advertised. I think the name was Propecius. I've been noticing my hair seems to be thinning on top lately, and I'd like to try it."

"Clinicians are increasingly feeling the impact of direct-to-consumer advertising of prescription drugs (DTCA). While advertising prescription drugs directly to consumers is not allowed in Canada, patients see newspaper reports, US ads, ads directed at health professionals, etc. In Canada, the average practicing physician can expect to get 10 specific drug requests per week, some of which would be for advertised drugs. In the United States DTCA appears to increase sales."

[Read the entire story on *Therapeutics Initiative's* web site: [www.ti.ubc.ca/](http://www.ti.ubc.ca/)]

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## DTCA IN THE EUROPEAN UNION?

### *A bad move*

A pilot system might be introduced throughout the European Union that would enable pharmaceutical companies to provide information directly to patients. This proposal was among several announced in July by Erkki Liikanen (European Commissioner for Enterprise and the Information Society) (1) as part of a proposed review of European Union pharmaceutical legislation. The pilot scheme focuses on three disease areas: AIDS, asthma and diabetes, chosen because they are long-term and chronic and because the types of drugs used for treatment are the same throughout Europe. The justification for the change given by Mr Liikanen is that currently European patients looking for information about their diseases and medicines are forced to rely on

information produced by companies outside Europe through the Internet, creating a differentiation between patients, e.g. between those who have access to the Internet and those who do not. The proposal requires the pharmaceutical industry to follow a code of conduct, with the European Medicines Evaluation Agency ensuring compliance with the code. Mr Liikanen stressed that the proposal does not amount to direct to consumer advertising. "We are not introducing advertising for prescription drugs", he said. However, some representatives of the UK pharmaceutical industry see this proposal as "opening the floodgates" (Pharmaceutical Marketing, August 2001), while organisations such as HAI and the UK Consumers' Association see the proposal as the thin end of the wedge to open the door towards direct-to-consumer advertising.

Other proposals that were announced, that aim to speed up the availability of new products and cut red tape, include:

- introducing a "fast-track" registration procedure for products of "significant therapeutic interest";

- introducing a conditional marketing authorisation in particular cases when there is a specific and identified patient need. This will allow the authorisation of new medicines on the basis of sufficient, but perhaps no definitive scientific data;

- abolishing the requirement to renew a marketing authorisation every 5 years. This will be "largely compensated for by a strengthening in pharmacovigilance requirements" with an "obligation for companies to monitor and analyse all adverse reactions".

(1)Mr Erkki Liikanen "Commission's proposal to review EU pharmaceutical legislation" speech/01/354, Brussels, 18 July 2001, available on EU Commission website at: [http://europa.eu.int/comm/index\\_en.htm](http://europa.eu.int/comm/index_en.htm)

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# DIRECT ADVERTISING OF PRESCRIPTION DRUGS ON THE AGENDA IN EUROPE

## THE UK CONSUMERS' ASSOCIATION HAS TAKEN POSITION

*The UK Consumers' Association has produced a policy report on direct-to-consumer advertising. Publication of the report was planned to coincide with an expected announcement from the European Commission of plans to relax the rules for advertising medicines in the European Union (see page 3).*

*We reprint extracts from the Briefing Paper published by Consumers' Association. The full briefing is available at: <http://www.which.net/campaigns/health/drugs.html>*

(...)

**The European Commission** is currently preparing to debate proposals which will relax the current restrictions on direct to consumer advertising of prescription drugs (DTCA).

*Consumers' Association's* report, *The promotion of prescription drugs: public health or private profit?* casts a critical eye over whether information provided by drug companies constitutes good quality patient information and the potential impact that this policy shift could have on the NHS.

(..)

**There is a growing debate** concerning how much information about prescription drugs

should be made available to patients – and who should be responsible for providing this information. While advertising prescription medicines to consumers is not currently permitted in the UK, drug companies are arguing that times have changed and that they should be able to communicate directly with patients about their prescription-only products. The question of whether the ban should be lifted is now very much on the agenda, with the European Commission currently undertaking a wide-ranging review of EU rules on the authorisation of pharmaceutical products and the provision of information to consumers.

(...)

**Consumers' Association's Health Survey** (May 2001) found that only 6 per cent of the 1,897 adults questioned trusted drug companies as a source of information, yet current deliberations at the UK and EU policy level about patient information in this area are dominated by the pharmaceutical industry's perspective. If this debate is not expanded to include a full assessment of this issue from the patient and public perspective, the UK may well see the introduction of DTCA with potentially disastrous consequences for patients, the wider public

and the NHS.

(...)

**The UK Government and European Commission** must urgently engage the public in the debate about advertising of prescription drugs, which is currently being driven entirely by industry. At present, policy developments are being driven by industry interests to the total exclusion of the public interest. This also raises a question about whether the Department of Health can properly balance pharmaceutical industry interests with the interests of patients and the public. The roles and responsibilities of the Department of Health in this area must be reviewed.

(...)

**Patient groups** must carefully consider their relationships with drug companies and ensure that they have robust policies in place to safeguard their own independence. As patient groups are increasingly becoming a source of information about drugs and treatments, the practice of drawing up guidelines to frame these relationships needs to become more widespread within the patient group community, with guidance and support from the Charity Commission.

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## LA REVUE PRESCRIRE

### DEBUNKS THE NOVELTY FACTOR

**Y**ear after year, drug companies flood the market with "novelties". Anything goes when it comes to motivating a sales force, attracting attention, or gaining new market shares: a simple name change, resurrection of an old product, new packaging, and so on.

Common sense, backed up by a reasonable memory and some reliable information, is enough to avoid being snared. No, novelty does not always mean innovation. However eye-catching the name or colour, a me-too product can hardly be heralded as a real innovation.

New drug substances, new manufacturing processes, or new routes of administration are often qualified as "innovations" by manufacturers and drugs agencies alike. But do they represent true therapeutic advances?

The yardstick by which purported innovations must be measured is the degree of extra benefit actually felt by the patient, not the degree to which these changes swell a company's coffers.

Take, for example, this year's review of our New Products column: among 500 or so "novelties" we examined in our French edi-

tion in 2000, there were dozens of "industrial" innovations but few real therapeutic advances.

The main problem is that the bulk of clinical pharmaceutical research is organised and funded, directly or indirectly, by drug companies. And shareholders are just as likely as others to believe that announcements of "novelties" are real therapeutic advances.

It is perfectly reasonable that pharmaceutical companies should strive to innovate. But, when true innovation is in short supply, too many companies exploit the "novelty factor" to lure patients, health professionals and the media.

[Taken from Prescrire International April 2001]

# EU CENTRALISED PROCEDURE DOES NOT MEAN A DRUG IS "INNOVATIVE"

Market authorisation can currently be granted at the European level in two ways. The "centralised" procedure is based on the opinion of the European Committee for Proprietary Medicinal Products (CPMP) and the decision of the EC Commission. The "mutual recognition" or "decentralised" procedure is based on recognition by other countries of authorisation granted by another member state.

It is often said that drugs granted marketing authorisation through the centralised procedure are, by definition, innovative. This is wrong.

**Production by biotechnics does not mean therapeutic advance.** The centralised procedure is compulsory for drugs produced by biotechnology (a,b)(1). The centralised procedure is optional for drugs mentioned in annex B of regulation n° 2309/93/EEC, manufacturers being free to choose which procedure they use (1).

The mode of production may be considered technically innovative, at least the first time it is used. But a glance at our New Products columns shows that these drugs do not always provide patients with a tangible advantage relative to available treatments.

**Industrial interests have superseded patients' interests.** As for drugs mentioned in annex B of regulation n° 2309/93/EEC, it is interesting to examine the changes in their definition with time.

Directive n° 87/22/EEC of 22 December 1986, which is the basis of European harmonisation for the centralised procedure, comprises a first version of annex B. As well as some particular drugs (radioisotopes) or manufacturing processes (two-dimensional electrophoresis), it defines as "innovative" drugs "medical products containing a new substance or an entirely new indication which, in the opinion of the competent authority concerned, is of significant therapeutic interest" (2).

But in regulation n° 2309/93/EEC of 22 July 1993, the sentence becomes: "Medicinal products intended for administration to human beings, containing a new active substance which, on the date of entry into force

of this Regulation, was not authorized by any Member State (...)" (3).

"Significant therapeutic value" disappears, along with the authorities' opinion of the therapy. This change in wording marks a switch of emphasis from the patient's to the industry's best interests.

The market now contains "me-toos" and drugs that have no innovative value (from the patient's viewpoint) but still carry the "European marketing authorisation" seal of approval, opening wide the door to the European market.

©PI

a- Directive n° 87/22/EEC: "(...) Whereas high-technology medicinal products requiring lengthy periods of costly research will continue to be developed in Europe only if they benefit from a favourable regulatory environment, particularly identical conditions governing placing on the market throughout the Community (...), the scientific expertise available in each of the national

authorities is not always sufficient to resolve problems of high-technology medicinal products" (ref 2).

b- Still called "biotechnologies", they can, according to regulation n° 2309/93/EEC, use recombinant RNA, coding genes, hybridomas or monoclonal antibodies (ref 3).

1- Commission européenne "La réglementation des médicaments dans l'Union européenne - Volume 2A - Avis aux demandeurs - Médicaments à usage humain" Eudralex, Luxembourg 1998: 2.

2- "Council directive 87/22/EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology" Official Journal L 015, 17/01/1987 p. 0038-0041.

3- "Council Regulation (EEC) n° 2309/93 of 22 July 1993 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products" Official Journal n° L 214, 24 August 1993: 1-21.

## Our judgements on products approved through the EU centralised procedure in 2000 (1)

| Prescriber's judgements (2) | Number | INN and brand names   |
|-----------------------------|--------|---|
| Bravo                       | 0      | -   |
| A real advance              | 0      | -   |
| Offers an advantage         | 3      | infliximab (3), nevirapine (4), ribavirin   |
| Possibly helpful            | 3      | abacavir, infliximab (5), lamivudine  |
| Nothing new                 | 11     | daclizumab, docetaxel (6), emedastine, eptifibatide, follitropin alfa (7), leflunomide, rabeprazole, repaglinide, telmisartan, temozolomide (8), toremifene |
| Not acceptable              | 0      | -   |
| Judgement reserved          | 1      | palivizumab   |
| Total                       | 18     |   |

1- We excluded products approved through the mutual recognition procedure.

2- See page 49 for details on our rating system.

3- Approved for a first indication: Crohn's disease.

4- Approved for a new oral suspension form; the substance was already on the market.

5- Approved for a new indication in rheumatoid arthritis; the substance was already on the market.

6- Approved for a new indication in advanced non small-cell lung cancer; the substance was already on the market.

7- Approved for a new indication in male hypogonadism; the substance was already on the market.

8- The judgement applies to both indications (glioblastoma and astrocytoma) that were successively approved for temozolomide.

[Taken from Prescrire International April 2001]

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## SOME DRUG AGENCIES ARE MORE OPEN THAN OTHERS

In 1966 the United States passed the Freedom of Information Act, which gives the American public rights of access to government information.

The Freedom of Information Act (FOIA) was supplemented in 1996 by the Electronic FOIA Amendments, which aimed to provide Internet access to all government files that have been requested in the past, and those that are likely to be requested in future. The Public Citizen consumers' organisation has examined the consequences of this law on freedom of drug information (a)(1).

The Food and Drug Administration (FDA) must make available the information it holds and to answer information requests, especially on efficacy and safety. The FDA website meets this obligation (b). The FDA has 20 days to answer requests for information. In the event of refusal, an appeal must be answered within a further 20-day period. A new refusal, or failure to respond within this period, opens the way to legal recourse.

The FDA can refuse to divulge information, usually because it involves 'trade secrets and confidential commercial information'. Trade secrets are fairly well defined, as 'a secret, commercially valuable plan, formula, process or device'. The definition of confidential commercial information is less precise, generally covering information that can be useful to competitors.

According to Public Citizen, the FDA asks manufacturers to define secret or confidential information, and the two parties then jointly defend the refusal to divulge the information before a judge. A law established in 1974 requires American government agencies, including the FDA, to create a descriptive index of files considered confidential.

It is possible to access information even before drug approval, in particular the minutes of experts. Backed by the Freedom of Information Act, Public Citizen gained the right for the public to access the file submitted to the experts about a new drug.

Although the FDA is not totally transparent and independent, American citizens do have a say.

Few countries have laws that give similar power. In Europe, Scandinavian countries are among the most concerned with transparency. In Sweden, the public has access to all data whose release is not explicitly forbidden by the 1980 Act on Secrecy, which covers national security, monetary policy, and the rights of citizens (c).

The European Medicines Assessment Agency (EMEA) publishes assessment reports when it grants marketing authorisations through the centralised procedure, but they are far from relevant (2,3). Few pharmacovigilance data are released, and marketing authorisation granted through the mutual recognition procedure is a "black hole" from which no public information escapes (3).

In France, The Agency for Health Product Safety is secretive and out of touch.

In 1996 the Uppsala Declaration, produced by a working group convened by Health Action International and the Swedish foundation Dag Hammarskjöld, called for more transparency in drug regulation (4). In

1997, the Erice Declaration called for improvements in public information on drug safety (5). American experience shows that transparency is possible, and that many advances in public access to government-held information have been gained only by constraint, and must continually be defended.

[Taken from *la revue Prescrire* May 2001]

a- Public Citizen is a non profit-making consumer organisation that represents the "eyes and ears of consumers in Washington". One of its chapters, the Health Research Group, works on health and drugs. Public Citizen publishes a drug bulletin entitled *Worst Pills, Best New Pills*, which is a member of ISDB. The website of Public Citizen can be consulted at <http://www.citizen.org>.

b- FDA website: <http://www.fda.gov>.

c- Swedish Medical Product Agency: [http://www3.mpa.se/ie\\_engindex.html](http://www3.mpa.se/ie_engindex.html)

1- "USA - Freedom of information act (FOIA)" *ISDB Newsletter* 2000; **14** (1): 9-12.

2- International Society of Drug Bulletins "ISDB Assessment of nine European public assessment reports published by the European Medicines Evaluation Agency (EMEA)" *ISDB*, Paris 1998: 12 pages.

3- "The failings of the European Medicines Evaluation Agency" *ISDB Newsletter* 2001; **15** (1): 6 pages.

4- "Statement of the International Working Group on Transparency and Accountability in Drug Regulation". [available on request]

5- "The Erice Declaration" *Prescr Int* 1998 ; **7** (38) : 191.

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## DIRECT-TO-CONSUMER ADVERTISING

### The New Zealand Situation

New Zealand and the USA are the only developed countries to allow prescription medicines to be advertised directly to the general public, an arrangement known as direct-to-consumer advertising (DTCA). This scheme is currently under the spotlight in New Zealand with a Government policy review underway.

The reason that DTCA developed in New Zealand was because of an ambiguity in existing laws which did not ever explicitly prohibit the advertising of prescription drugs to the public. The current regulatory framework for the scheme relies on industry self-regulation, however judicial action can be taken if advertisements do not comply with legislation covering medicines, fair trading,

commerce, consumer guarantees etc.

Expenditure in New Zealand on prescription DTCA is estimated to be NZD\$18m in 2000, up 24 percent on 1999. Of this, 61 percent was spent on television advertising and 30 percent on advertising in magazines.

The enthusiasm of the pharmaceutical industry for DTCA is not hard to understand. The advertising of one prescription drug to consumers in the USA helped increase its sales twenty-three fold over seven years from approximately USD\$240 million to USD\$5.6 billion.

There are many arguments put forward to support and justify DTCA. These are often couched in terms of the public having a moral "right to know", freedom of speech, the rights of suppliers in a market place.

A major argument for DTCA is that it results in a better informed and empowered public who will be encouraged to discuss often sensitive issues with their doctor. Realistically, the effect of the advertising is that it creates an indiscriminate demand by consumers for a product and it is then up to prescribers to explain whether or not prescription of the product is appropriate. Not unexpectedly, research shows that the doctor under these circumstances usually accedes to the patient's request.

There are many medical and financial arguments against DTCA including one that health is not a normal market place. It does not have the usual checks and balances and normal promotional tools may therefore not be appropriate.

However, the most important issues should be those that reflect the needs of consumers.

Surely the fundamental issues are public health and helping consumers make suitable decisions about their own health. Consumers can only be expected to make intelligent choices if there is appropriate and reliable information about relevant issues including:

understanding of the health problem, ie underlying condition,

the various options for management, and the risk/benefits of each of the options.

Such information is not found in advertisements.

Advertising is focussed on medications and suppliers are naturally committed to selling their own products. Advertising is expensive and its desire to inform often extends only to those products that generate high profits. The only rewards are for sales. Thus, to promote products, advertisers naturally tend to under-emphasise risks and adverse effects. There is no incentive to provide any surrounding information. Naturally, pharmaceutical industry advertising ignores whether pharmaceuticals are the most appropriate course of treatment and also other pharmaceuticals that may treat the condition just as well.

For commercial pharmaceutical companies their desired rewards and *raison d'être* are profit and sales. It is naïve and fallacious to assume that commercially driven advertising can be self-regulated - restraint and balance are not rewarded

As for consumers, they are being targeted when they are unwell, at their most vulnerable and least able to make a decision on personal health issues.

The review of DTCA in New Zealand will be interesting. PHARMAC, the Crown Entity that manages the New Zealand Pharmaceutical Schedule on behalf of the Government, actively supports a review of the legislation regulating DTCA. It is opposed to advertising of prescription medicines direct to the public and has stated it would like to see an outcome that considers the best outcome for patients and taxpayers. Its concerns are both financial and medical.

Questions have been raised about the body set up by the New Zealand Ministry of health to monitor the advertisements. In addition, it has been said that the current system of voluntary review is quite unsatisfactory and that it is inappropriate for the industry body, the Association of New Zealand Advertisers to act as judge and jury when it is a direct beneficiary of DTCA.

Mary Hemming

(*Therapeutics Guidelines Limited*)

## NEWS OF BULLETINS

### NEWS OF *LA REVUE PRESCRIRE'S* REPS MONITORING NETWORK

#### Pretences and off-label claims

- **Information increasingly unrelated to the summary of product characteristics (SPC).**

The annual report by Prescrire's Medical Representatives Monitoring Network sometimes provokes strong reactions, especially from the pharmaceutical industry (1,2). Yet the trends observed by this strict sentinel network are so distinct that they can hardly be due to chance alone (3,4).

During the period spanning March 2000-March 2001, the questionnaires collected by the network's observers showed a global deterioration in the quality of medical visits.

**More frequent promotion of off-label indications.** Prelaunch visits (presenting drugs that have not yet been marketed) were less frequent than in previous years (4% of observed visits, compared to 5% the year before and 11% the year before that). We assume that this is because prelaunch campaigns are increasingly aimed at hospital physicians and the general public (even prescription-only drugs), rather than at primary care physicians.

In all, 55% of visits focused on newly marketed preparations and 45% on older drugs. There was a trend towards promotion of off-label (i.e. not recommended in the SPC) indications and dose regimens for older preparations.

Only 68% of indications promoted by the reps conformed to the corresponding SPC (compared to 79% in 1997, with a gradual decline). As regards the recommended doses stated by the reps, 86% conformed to the SPC, 11% were slightly different and 3% were totally different.

**Risks increasingly overlooked.** The reps stated contraindications in only 10% of cases (against 17% the year before); and warnings in only 10% (against 14% the year before). Drug interactions were stated in only 8% of cases and were denied in 6% of cases. As for adverse effects, they were stated in only 10% of cases and denied in 9% of cases (against 4% the previous year).

Some reps seem to think that prescribers should know the risks associated with older drugs, and that these do not need to be restated (2). This is not the opinion of the network observers, who considered this year that, in 86% of cases in which risks were not mentioned, they should have been stated.

**Official documents not presented.** Medical reps were less likely this year to offer documents (including brochures) on the drugs they were promoting (only 17% of cases). A very small number of observers received the statement from the Transparency Commission that places the drug in context with other members of its class. In France this statement is based on a scoring system assessing improvement in the "medical service rendered" (effectiveness). It was presented in only 2% of cases in 2000-2001, while in previous years this percentage had been increasing (albeit remaining below 10%). Some reps even appeared to be unaware that the statement existed, while others said they did not have a copy to hand or that the document was "unavailable". Some offered to send it, but never did. [Note that it is a legal obligation for medical visitors to supply this document in France.]

**Fewer gifts?** As regards the small gifts given by many medical reps, members of the Network continued to receive very few: in 11% of visits in 2000-2001 doctors were offered paperweights and other gadgets, bottles of wine, invitations to dinners or social programmes, and a few were offered paid education. The fact that this percentage is lower than in previous years does not mean that visits are becoming more serious and more informative. Rather, visits to members of the Network are probably unrepresentative: Network observers are often listed as "Prescrire readers" or even worse "Outstanding readers of Prescrire Readers' test", meaning that they tend to ask technical questions, disdain gifts, and reject invitations. The reps simply adapt their presentation to the type of audience...

**Enough is enough!** The mean global score for reps' visits (attributed by the Network observers using a visual scale) was no more than 5/10. The worst mean score (1/10) was for Pfizer reps touting fluconazole powder for oral suspension, mainly because reps claimed false indications (com-

plications of antibiotic therapy, denture use, steroid inhalation, dry mouth etc.), and emphasised the orange flavour. This is one of the examples that most annoyed the observers, especially as this is a drug that must be used with caution.

[ Adapted from *la revue Prescrire*  
June 2001]

**Selected references from Prescrire's document watch.**

- 1- Prescrire Editorial Staff "Sales representatives : a damning report by Prescrire reps monitoring network" *Prescr Int* 1999; **8** (41): 86-89.
- 2- Prescrire letters to editors "Courriers: Visite médicale - Réactions, commentaires et discussions" *Rev Prescr* 1999; **19** (196): 472-475.
- 3- Prescrire Editorial Staff "News of Prescrire reps monitoring network" *Prescr Int* 2000; **9** (46): 49.
- 4- Prescrire Rédaction "Risques occultés" *Rev Prescr* 2000; **20** (207): 432-433.

**Pay your membership fee!**

You will soon receive a request for your membership fee for 2001. Please pay as soon as possible. ISDB's activities depend on your contribution.

**ISDB**



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# THE AUSTRALIAN PHARMACEUTICAL BENEFITS SCHEME (PBS): RECENT DIRTY TRICKS

## *Therapeutic Guidelines Limited*

The Australian Pharmaceutical Benefits Scheme (PBS) commenced 52 years ago. At that time, there was concern that many people could not afford expensive but valuable new drugs such as penicillin. A Pharmaceutical Benefits Advisory Committee (PBAC) was set up; they recommended that a limited list of life saving or disease-preventing drugs should be made available for prescription free of charge. The World Health Organization subsequently adopted this concept as a key mechanism of ensuring equity of access to necessary drugs.

The PBS has evolved from a scheme that fully subsidised 139 drugs to one that now partially subsidises about 620. Over the years, the cost of the PBS has escalated and patient co-payments, brand premiums and other strategies have been used to provide price signals and transfer some of the cost to consumers. The PBS purchases about 90% of all prescription medicines. This monopoly power has resulted in Australian drug prices being substantially lower than the OECD average while still retaining access to a comprehensive range of medicines. This has been good for Australian consumers but it has caused the pharmaceutical industry considerable angst.

In 1948/1949 the PBS cost the government \$298,074. It took 40 years for the costs to reach a billion dollars but more recently costs have been rising far more rapidly. In 1999/2000 the PBS cost the government \$3.45 billion, an increase of 16% on the previous year. The 2001 budget papers estimated PBS expenditure for 2000/01 to be \$4.26 billion, a 21% increase on the previous year. This cost escalation is unsustainable. It also has opportunity costs; less money is available for other areas such as public hospitals, aged care and public health.

There are a number of reasons for escalating PBS costs. There are increasing numbers of aged people with chronic conditions that can genuinely benefit from pharmacological intervention. There have been national cam-

paigns to improve the treatment of inadequately treated conditions such as asthma, depression and elevated blood cholesterol levels. There has been State-Commonwealth cost shifting, with hospitals limiting supplies of drugs when patients are discharged and privatising outpatient clinics and pharmacies. But the major cause of increased PBS costs has been a shift towards prescribing larger volumes of newer, more expensive medication compared to older, cheaper drugs. Not only has this use not always accorded with clinical best-practice guidelines; many of the prescriptions written for these drugs are for uses that have never been approved by the PBAC as cost-effective. In many cases the PBS is paying a price for these expensive medications that is far higher than would be justified by the health benefit achieved.

The pharmaceutical industry is the main driver of the increasing costs. According to the industry's own figures, manufacturers spend up to one-third of sales revenue on marketing, twice as much as they spend on research. Marketing programs involve pervasive advertising, large numbers of sales representatives, physician hospitality and international trips, conference sponsorships, lavish drug launches, gifts and gimmicks. The pharmaceutical industry has also infiltrated government-promoted prescribing software with advertisements for the latest and most expensive drugs; these now flash in the physician's face at the time of prescribing. Over the last few years, individual pharmaceutical companies have sued PBAC members over decisions not to list drugs such as sildenafil (Viagra®), they have successfully lobbied the Federal Health Minister to replace PBAC members judged antagonistic to industry and have succeeded in getting a former industry lobbyist appointed to the committee.

Minister Wooldridge has argued that these changes to the PBAC have resulted in a better committee that now contains industry expertise. Critics see his interference as the latest pro-industry initiative of the Howard government. They argue that adding an industry lobbyist to the PBAC is akin to

placing the defendant on the jury, is likely to inhibit free debate among independent experts and could result in more costly drugs (with more marginal benefits) being added to the PBS. This, in turn, would lead to an even greater PBS cost blow-out that the government would inevitably pass on to consumers via higher co-payments, de-listing "less-essential" drugs and other strategies. The end result would be a U.S. style pharmaceutical system where poorer citizens could no longer afford necessary drugs.

Another battle is over direct-to-consumer advertising (DTCA) of prescription drugs. The Australian Pharmaceutical Manufacturers Association (APMA) is lobbying the Federal government to remove current restrictions on DTCA of prescription drugs. The U.S. experience shows why. In 1999, U.S. pharmaceutical companies spent \$US 1.8 billion on DTCA, a 40% increase over 1998 with U.S.\$ 1.1 billion spent on television ads, a 70% increase over 1998. Forty one percent of DTCA spending was concentrated on ten products, among them loratidine (Claritin®, \$137 million), finasteride (Propecia®, \$100 million) and sildenafil (Viagra®, \$94 million). The 25 top-selling DTCA drugs accounted for 40.7%, or \$7.2 billion, of the overall \$17.7 billion (19%) increase in drug sales (retail) in 1999 compared to 1998. Doctors wrote 34.2% more prescriptions in 1999 than in 1998 for the top 25 DTCA drugs. Doctors wrote only 5.1% more prescriptions for all other prescription drugs.

Over the last 10 years a variety of strategies have been employed in Australia to try to improve medicinal drug use. The Pharmaceutical Health and Rational Use of Medicines (PHARM) Committee recommended a quality use of medicines (QUM) policy as the final integrating arm of national medicinal drug policy. They advocated independent information; drug audits and targeted education aimed at both consumers and health providers. PHARM was successful both in gaining small amounts of funding for QUM projects and in proving that certain strategies worked. A Liberal ►►

► government then set up a National Prescribing Service (NPS) in addition to PHARM. The NPS works with Divisions of general practice and has primarily focused on educating prescribers. For an expenditure of about \$5 million per annum they have demonstrated improvements in prescribing worth about \$15 million per annum. While NPS activities are undoubtedly worthy, the savings achieved represent less than 2% of latest \$800 million annual increase in the cost of the PBS. The 2001 federal budget provided another 4 years funding for the NPS (at the same level) and also allocated \$14.6 million (over four years) for “a consumer education strategy “. The danger of the latter initiative is that it could lead to yet more fragmentation and duplication of effort, especially if another implementing body is set up.

The changes made to the PBAC by Minister Wooldridge, and the escalating costs of the PBS, have resulted in unprecedented media coverage<sup>1,2</sup> and considerable industry and political skulduggery.

Martyn Goddard was a consumer representative on the PBAC; he is well known in Australia as a journalist and AIDS activist. He tried harder than anyone to hold together the remnants of the old committee, but after an industry representative was placed on the PBAC he resigned and became an outspoken critic of the present government and the industry. He was then dropped from all his committee advisory and consulting roles with no warning or justification.

Professor David Henry is a pharmaco-economic expert who played a key role in introducing economic analysis to the PBAC. He was eliminated from the committee when it was reconstituted by Ministerial fiat. After David appeared on an ABC-TV investigative program, federal health department officials were ordered to retrieve all documents relating to him. Subsequently, confidential documents were released to a public relations company and then to news outlets with an accompanying written commentary implying that David had taken money from a pharmaceutical company and biased PBAC decisions in favour of that company's products (and against another's). Fortunately, good journalists quickly chased down the truth (the story was a complete fabrication and was easily disproved).

In late February 2001, three colleagues and I set up a university Web site containing

news articles and published cartoons relating to the PBAC affair. The material summarised the history and background to recent events and had links to published material that featured alleged relations between the federal health minister and the pharmaceutical industry. The web site also served as a forum for ideas as to how the PBS could be made sustainable. At the end of June 2001, the University shut down this web site without prior consultation with any of the academics involved on the grounds that it defamed the Federal Minister for Health. I also had a charge of serious misconduct brought against me. This charge was subsequently withdrawn but the web site remains down due to continuing legal and other action.

In short, there has been a systematic campaign in Australia to discredit former members of the PBAC and their supporters and curtail informed public debate about the PBS. The challenge for consumers, NGOs and parties contesting the forthcoming Australian federal election is to re-examine existing strategies and structures and formulate better ways of ensuring the sustainability of

the PBS. Strategies suggested include eliminating the former industry lobbyist from the PBAC, more rigorous PBS price / volume negotiations, more independent information, audit and other decision support functions incorporated into prescribing software, less pharmaceutical promotion (especially resisting DTCA), and budget holding or other forms of clinical governance to encourage physicians to prescribe more cost-effectively. In addition, many believe that new structures are required and that PHARM, the NPS, the PBAC and related bodies should be rationalised and reorganised.

[Ken Harvey, Councillor, Australian Consumer's Association and Director, Therapeutic Guidelines Limited. E-mail: k.harvey@bigpond.net.au]

1 Jackson L. Paying the price. ABC-TV Four Corners Program, February 19, 2001-08-09 <URL: [http://www.abc.net.au/4corners/stories/4Cprograms\\_PA\\_YINGTHE.htm](http://www.abc.net.au/4corners/stories/4Cprograms_PA_YINGTHE.htm) >

2 Coulthart R. The doctor's gravy train. Nine Network Australia Sunday Program, August 5 2001.<URL: [http://news.ninemsn.com.au/sunday/cover\\_stories/article\\_896.asp](http://news.ninemsn.com.au/sunday/cover_stories/article_896.asp) >

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## INFOPHARMA

# ISRAEL PRESCRIBING GUIDE 2001

Philip Sax, editor of the ISDB drug bulletin *Pharma (Israel Drug Bulletin)*, has launched a concise prescribing and dispensing guide for physicians and pharmacists.

Information is drawn from the manufacturer's product literature, medical and pharmaceutical literature, regulatory and health authorities.

Entries are listed in alphabetical order by generic names (a first in Israel), and are cross-indexed by brand names.

The Guide fills a gap in the poorly developed area of independent drug information in Israel, where only an industry-supported directory with the most basic information on names, ingredients, doses and indications, is available.

The Guide provides Israeli doctors with an independent reliable and professional source of information on dosage, contraindications, precautions, interactions, side effects, as well as reimbursability in the

major Sick Funds.

The major feature of the Guide is prescribing information on about 200 drugs of current interest and new drugs. This is precisely where the need is greatest for the physicians who are bombarded with reps and promotional material.

Philip Sax is already working on a second expanded edition of the Guide. The Guide, like the Bulletin, has drawn very favourable comments from key professionals. However, in the meantime as with the Bulletin, Philip Sax is left to finance alone the publication apart from sales of both the Bulletin and the Guide.

According to Philip Sax, this is indicative of the lack of interest and vision on the part of health care institutions whose job it is to ensure that medicines are used safely and effectively.

For more details you can contact Philip Sax: [saxp@netvision.net.il](mailto:saxp@netvision.net.il)

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## ON PSEUDO-INNOVATIVE DRUGS

*Restriction list for pseudo-innovative drugs improves therapeutic quality and reduces expenditures, says Arznei-telegramm*

Most of the so-called innovations of the pharmaceutical industry are without therapeutic relevance. They do not improve health care, even though marketing and sponsored opinion leaders may disagree. Only one purpose is reached: therapy becomes more expensive, and that is the only aim. Excessive material investments to gain higher returns and market shares undermine the quality and economic feasibility of the health care system, leading to higher dues for the national sickness funds. Counter-measures are needed.

Real therapeutic progress is rare. We estimate that there are at best not more than two interesting drugs per year in clinical medicine, but only one every second year in general practice. Such innovations need no advertising. They are easily recognized by industry-independent pharmaco-therapeutic expertise and promoted without financial investment. The same expertise allows to recognize marketing bluffs and to establish a "restricted list for pseudo-innovations".

The self-government of the German medical profession appears to be unable or unwilling to act due to the widespread corruption of medical opinion leaders. The executive federal committee formed by representatives of the medical profession and the statutory sickness funds are blocked by court order with regard to any activities to control the German drug market, since it has been sued by the pharmaceutical industry as an illegal syndicate, according to European law. This case has not been decided, yet, and therefore the committee cannot act on the establishment of a restricted list for pseudo-innovations. The activity of the German pharmaceutical industry is remarkable, abusing legal actions for their purpose. The reference price system established first in Germany and subsequently taken on by many European countries is being played down here: The annual savings for the statutory sickness funds have been reduced by the new reference price law from annually 650 million Euro to 325 million Euro to appease

the complaining drug industry.

The ministry of health is responsible to protect the citizens from ever increasing deductions to their statutory sickness funds caused by useless expenditures for pseudo-innovative drugs. Economic forces won't help, since they will create rising costs due to the fact that the financial input of the industry will prevent the process of quality-dependent product elimination.

### Pseudo-innovations undermine therapeutic quality

Preference of established standard drug regimens is not an indicator for unwillingness to follow scientific progress, but for therapeutic conscientiousness. Drugs with well documented, high levels of efficacy – usually no longer under patent protection and therefore low priced – may be lost, when they are replaced by promoted "innovations".

The clinical benefit of *Antidiabetic drugs* such as glibenclamide (EUGLUCON), insulin (HUMINSULIN) or metformin (GLUCOPHAGE) has recently been demonstrated by the UKPDS (United Kingdom Prospective Diabetes Study; a-t 1998; No. 10: 88-90). Now the industry starts to promote a large-scale switch to so-called innovations. *Glimepiride* (AMARYL; a-t 1977; No. 1: 2-3), available only for 5 years, leads today's market with more than 2 million prescriptions at 100 million Euro. Advertised grotesque statements such as "Physiologic, Harmonic"<sup>1</sup> stimulated sales. *Repaglinide* (NOVONORM) introduced late in 1998 is now costing more money than EUGLUCON, which is still the most prescribed (and most expensive) glibenclamide. The proven long-term benefits of glibenclamide have been effectively silenced by noisy marketing campaigns propagating marginal advantages of repaglinide such as more flexible food intake (a-t 1998; No. 11: 100-1).

Even more damaging are advertisements for the *Glitazones* which are pushed into the market by misleading statements such as "From the very beginning" *pioglitazone* (ACTOS). Glitazones including *rosiglitazone*

(AVANDIA; a-t 2000; 31: 66-7) are only licensed as adjuvant therapy in diabetes mellitus type 2 due to insufficient efficacy (a-t 2000; 31: 103). Potential to prevent diabetic complications such as cardiovascular disease was not tested for and checked before marketing authorization. Therefore, safety and efficacy of glitazones have to be regarded as questionable in view of published evidence, in spite of the advertised "new dimension"<sup>2</sup> in diabetic therapy. Inacceptable effects under therapy are weight gain during treatment and reports of cardiac and vascular adverse events and damages (a-t 2000; 31: 66-7 and 2001; 32: 64).

The tendency to increasingly prescribe *artificial (modified) insulins* cannot be explained by therapeutic advantages. Marketing strategies including questionable statements by the German Diabetic Society (a-t 2000; 31: 37-8) succeeded in achieving the second highest prescription rate for *insulin lispro* (HUMALOG) within five years only. Artificial insulins such as *lispro* and *glargin* (LANTUS; a-t 2000; 31: 108) show an increased receptor affinity to insulin-like growth factor IGF 1 and may, therefore, induce proliferating diabetic retinopathy and promote cancer (a-t 1999; No. 6: 66) – an unnecessary pseudo-innovation with a Damocletian Sword effect.

Pseudo-innovative drugs without any additional therapeutic effectiveness and with insufficiently tested long-term safety can be found among many therapeutic classes, e.g. *Alpha-adrenoceptor blocking agents*, *Calcium-channel blockers*, *Proton pump inhibitors*, *Thiazide diuretics*, *Loop diuretics* etc. (Table). New chemical structures such as *zolpidem* (BIKALM; a-t 1996; No.7: 72) or *Angiotensin-II receptor antagonists* rapidly turn out to be nothing but another variation of a well known agent.

*Angiotensin-II receptor antagonists* were first marketed in 1995. In 2000, already 3.8 million prescription units (combination drugs excluded) were sold at 385 million Euro, as compared to 19.6 million prescription units of ACE-inhibitors at 640 million Euro. A therapeutic benefit has been proven regarding stroke prevention, cardiovascular events, and reduced mortality rates only for ACE-inhibitors, but not for the much more expensive angiotensin-II receptor antagonists (a-t 2001; 32: 2). Prolonged life expectancy has been demonstrated for patients with heart failure when ►►

► treated with ACE-inhibitors, but not with angiotensin-II receptor antagonists (a-t 2000; **31**: 68-9). Patients suffering from ACE-inhibitor induced or other angio-edema cannot be switched to angiotensin-II receptor antagonists (a-t 1998; No. 11: 105). However, the latter drugs may be an alternative for the 3% of patients suffering from severe cough with ACE-inhibitor therapy.

The antiplatelet agent *clopidogrel* (ISCOVER, PLAVIX) has no place in routine therapy and belongs to a rather limited niche of indications. Treatment with clopidogrel is more than 50 times more expensive than with ASS (ASPIRIN). Therefore, its use may only be justified in patients showing serious contraindications to ASS (a-t 1998; No. 8: 70-1). It is without any relevant therapeutic advantage over ASS in the secondary prophylaxis of stroke (a-t 2001; **32**: 34). But it should replace its predecessor ticlopidine (TICLID), since it appears to be less toxic to bone marrow.

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#### *Administrative aspects*

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*Legislative measures for introducing a restricted list for pseudo-innovative drugs are not new to the German Social System. Laws already exist:*

- *The demand for economic guidance of medical treatment is instituted within social legislature (Sozialgesetzbuch V) as well as a legal basis for a restricted list of drugs (§ 34 SGB V).*
- *The law on reference pricing allows to fix the drug price for alternatives paid by the statutory sickness funds within the lower third of the price-range between lowest and highest product price.*

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#### **Possible savings**

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Examples shown in the table (for the year 2000) indicate that expenditures for drugs can be reduced by about 1.5 billion Euro if prescriptions are switched to proved alternative drugs of proven efficacy. This will also improve the quality of medical care for patients.

Professor U. SCHWABE presented similar figures at the Hearing of the *Deutsche Bundestag* on legislation concerning the medication budget for doctors working for the statutory sickness funds. He calculated that the expenditures for drugs financed by statutory sickness funds amounted to about

20 billion Euro in the year 2000 and that about 1.25 billion Euro can be saved by abandoning prescriptions of pseudo-innovative drugs (“analogues”).<sup>3</sup> Switching prescriptions completely to generic products will save another 1.5 billion Euro.<sup>4</sup> Therefore, expenditures for drugs can be reduced by more than 2.5 billion Euro or 13% of the total medication of the German statutory sickness funds. This money could be used as a refund to members of health insurance programs or for substantially innovative treatments without increasing health care costs for the patients.

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#### **Conclusions**

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**The intended reform of the German health care system should try to control the abundance of useless new drugs with questionable potential by extending the restriction list to pseudo-innovations.**

- **Pseudo-innovations impede therapeutic progress by consuming the financial means needed to finance sound therapeutic advances.**
- **The establishment of a restriction list for pseudo-innovations combined with generic prescribing will activate a reserve of more than 2.5 billion Euro without affecting the quality of health care.**
- **Quality and safety of drug treatment will improve by focussing on established therapeutic principles and avoidance of less thoroughly tested “new” drugs.**
- **These savings spare the public from increasing insurance premiums and the medical profession from claims for compensation.**

[Translated from the German bulletin *Arznei-telegramm* 2001; 32: 77-9]

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1 Hoechst: AMARYL-advertisement, *Ärzte-Zeitung*, Nov. 25, 1996

2 SK BEECHAM: Advertisement for AVANDIA, *Ärzte-Zeitung*, July 20, 2000

3 SCHWABE, U: Deutscher Bundestag – 14. Wahlperiode – 101. Sitzung, Gesundheitsausschuss, 27.06.2001

4 SCHWABE, U. in SCHWABE, U., PAFFRATH, D. (Hrsg.): “Arzneiverordnungs-Report 2000”, Springer, Berlin 2001, p 687-713.

# REPORTING RANDOMISED CLINICAL TRIALS: THE 2<sup>nd</sup> CONSORT STATEMENT

In recent months, major medical journals including *JAMA*, *The Lancet*, *The Annals of Internal Medicine*, and the *Canadian Medical Association Journal*, have drawn attention to the CONSORT Statement.

### What is the CONSORT Statement?

The Consolidated Standards of Reporting Clinical Trials (CONSORT) Statement comprises a checklist and a flow diagram intended to improve the reporting of randomised clinical trials (RCTs)

The first CONSORT statement was published in 1996 by *JAMA* (1). Since then many journals have endorsed this tool in their instructions to authors. In 1999, 13 members of the CONSORT group, including Glaxo, Abbot and MSD, met to revise and update the first Statement. The revised version has amended some items in the checklist and in the flow diagram (2).

**The checklist** includes 22 items from title and abstract to interpretation of the results in the context of current evidence. **The flow diagram** covers the following stages of a trial: enrolment, intervention, allocation, follow-up and analysis. It provides a clear picture of the progress of all participants throughout the trial.

### Implications for ISDB Bulletins:

CONSORT is an attempt to promote minimum standards in the reporting of randomised controlled trials. The first version was not very demanding. The second one is better, but still leaves room for improvement. For instance there is only one item on the reporting of adverse effects (severe ones); approval by ethics committees and declaration of financing are not *required* but desirable.

To sum up, a randomised controlled trial report that does not meet CONSORT requirements is really bad; and a report that meets them may still omit important points and should be further examined, as many items remain to be checked. The CONSORT Statement is therefore a minimum requirement for reporting randomised controlled trials. It can help in the appraisal of

randomised controlled trials that assess efficacy and safety of medicines, in that it allows a better understanding of the study and easier identification of possible biases.

Some of the major journals involved in CONSORT have acknowledged that only a minority of the RCTs they publish follow CONSORT requirements. ISDB editors urge these journals to apply CONSORT requirements more rigorously when they receive submissions of trial reports.

## GOOD SOURCES

### DRUG REGULATION IN EUROPE

**We strongly recommend the two following reference sources on drug regulation in Europe. The fact that an inside critique of the system and an outside review are consistent give much weight to the arguments.**

\* Silvio Garatini and Vittorio Bertele, both member of the Committee for Proprietary Medicinal Products (CPMP), have published an inside review of the way the European Medicines Evaluation Agency (EMA) operates.

In their conclusion, they recommend that *"The institutional location of EMA should be changed so it reports to the directorate of public health, not industry [Editor's note: EMA is located at DG Enterprise]. Approval of new drugs must involve comparative assessments. More criticism is needed in the approval of new drugs. To defend patients' interests, companies cannot be allowed to release drugs with the sole aim of obtaining a slice of the market. The increasing power of the pharmaceutical industry requires an equally strong counterpart to ensure that drugs continue to be beneficial to patients,*

If regulatory bodies were also to incorporate the CONSORT requirements in their regulations, that would do a lot more to improve standards.

[This piece was initially written by Maria Font (*Dialogo sui Farmaci*), and reviewed by the persons listed in the colophon on page 14]

1- Begg C, Cho M, Eastwood S et al "Improving the quality of reporting of randomized controlled trials" *JAMA* 1996; **276**:637-639.

2- David Moher, Kenneth F Schulz, Douglas G Altman, for the CONSORT Group\* "The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials" *Lancet* 2001; **357**: 1191-4. [The revised CONSORT statement is also published in *JAMA* 2001; **285**: 1987-91 and *Ann Intern Med* 2001; **134**: 657-62.]

*and are not just a profitable business."*

Silvio Garatini and Vittorio Bertele "Adjusting Europe's drug regulation to public health needs" *Lancet* 2001; **358**: 64-67.

\* John Abraham and Graham Lewis have published a book investigating how medicines are controlled in Europe. One of their main arguments is that *"the drive to produce and approve more drugs more quickly for a single European market dominates other considerations, such as improvement in democratic accountability, the independence of regulators and scientific expertise from commercial interest, and drug safety testing and surveillance."* In chapter 7 "Democracy, technocracy and secrecy" they notably draw on ISDB's critiques of the European Public Assessment Reports (EPARs). They quote the ISDB survey to assess the degree of transparency of drug regulatory agencies that was published in 1996 in the *International Journal of Risk and Safety in Medicine*, which led to the Uppsala Declaration.

John Abraham and Graham Lewis "Regulating Medicines in Europe - competition, expertise and public health" Routledge London and New York 2000.

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## E-DRUG ELECTRONIC CONFERENCE

E-Drug is SATELLIFE's electronic conference on essential drugs. E-Drug is used by professionals in this field to obtain and discuss current information on essential drugs, including national policies and standard treatment guidelines. Members also use E-Drug to announce and learn of upcoming conferences or courses in this vital field. We recommend this source of information to all ISDB editors; see E-drug website to subscribe.

[<http://satellife.healthnet.org/programs/edrug.html>]

SATELLIFE is an international not-for-profit humanitarian organisation employing satellite, telephone, and Internet technology to serve the health communication and information needs of countries in the developing world through a global computer-based communications network, *HealthNet*.

SATELLIFE's mission is to improve health by enhancing connectivity among professionals in the field via electronic communications and exchanges of information in the areas of public health, medicine, and the environment. A special emphasis is placed on areas of the world where access is limited by poor communications, economic conditions, or natural disasters.

[<http://satellife.healthnet.org/index.html>]

We reprint a recent E-drug posting on quality and use of drugs

Access to essential medicines is only part of the problem

In recent times, we have put a lot of concern on access to life-saving and life-prolonging medicines. I think that we have forgotten about the quality of those drugs and their proper use.

I have a view. Let us concentrate on the whole: Quality, access and proper use. These 3 aspects must be emphasized together. If we continue emphasizing access alone, we shall rejoice for a while and mourn for a longer time.

With that view, can't we have policies and facilitation in developing countries to stress: quality of generics, access to quality generics and proper use of high quality generic medicines?

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The ISDB Newsletter is sent free of charge to ISDB members and corresponding members.

### IMPORTANT!

#### Inform us of your new e-mail address

Some of you have changed e-mail addresses over time. You may therefore miss electronic messages we circulate to the membership.

Please could you inform the executive committee whenever this happens;

Maria Font (General Secretary) [mfont@nettuno.it](mailto:mfont@nettuno.it)

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## NO FREE LUNCH FARMACEUTICAL FACTS

*No Free Lunch* is a US organisation that encourages health care practitioners to 'just say no to drug reps'. ISDB bulletins should encourage readers to do the same. Their website ([www.nofreelunch.org](http://www.nofreelunch.org)) deserves a visit. They have collected facts and figures about advertising, research and development.

According to industry estimates, promotional spending reached a record high \$13.9 billion dollars in 1999, an 11% increase over 1998. The amount actually spent on promotion is much higher than this — higher in fact than is spent on research and development.

Direct to consumer advertising accounted for 13% of this total, or \$1.8 billion dollars in 1999; it will likely surpass \$2 billion dollars in 2000. (National Institute for Health Care Management)

41% of DTC spending in 1999 was concentrated on ten products, among them Claritin™ (\$137.4 million), Propecia™ (\$99.7), Viagra™ (\$93.5), Prilosec™ (\$79.5 million), and Xenical™ (\$75.6). The target of DTC ads: overweight, impotent, balding men with heartburn and sinus problems.

In 1998, Schering-Plough spent \$136 million on advertising for Claritin™. This is more than the Coca-Cola Company spent advertising Coke™ and more than Anheuser-Busch spent advertising Budweiser™.

Over \$6 billion dollars were spent on details (drug rep visits) to physicians in 1999, an increase of 6.5% over 1998. Fifty-nine million details were made in 1998. One million, two hundred and twenty-six thousand details were made for the antibiotic Trovan™ alone, which was the most promoted drug in the U.S. in 1998. Its sales in its first 12 months were the most ever for an antibiotic in the U.S. Its use has since been limited by an FDA advisory following reports of severe liver toxicity. (FDA Public health advisory).

The pharmaceutical sales force grew from about 35,000 sales representatives in

1994 to more than 56,000 in 1998. (Scott-Levin Consulting). That's nearly one drug rep for every 11 practising physicians in the U.S.

The number of pharmaceutical company sponsored events (e.g., dinners) increased from 70,000 in 1993 to 280,000 in 1999. Celebrex™ was promoted through 3,445 events, Vioxx™ 3,393. Pfizer spent \$135,000,000 on meetings and events (e.g., dinners). (Scott-Levin Consulting)

In the first six months of 2000, 7,600 Pfizer reps made 4, 197,000 details. One in seven meetings/events (e.g. dinners) were sponsored by Pfizer. (Scott-Levin Consulting)

In a study by Avorn, et al, forty-six percent of physicians reported that drug reps are moderately to very important in influencing their prescribing habits (Amer Journal of Med, 1982).

In a study by Lurie, et al, one-third of medical residents reported that they change their practice based on information provided by drug reps (Journal of Gen Int Med, 1990).

Pharmaceutical companies provided \$7.2 billion dollars worth of free samples to doctors' offices in 1999, up from \$6.6 billion in 1998. (National Institute for Health Care Management)

Schering-Plough gave out 35.7 million samples of Claritin in 1999. A month's supply of Claritin costs \$68 dollars. A month's supply of chlorpheniramine costs 62 cents. (American Medical News)

A study by Chew, et al (JGIM, 2000), found that in the treatment of hypertension, over 90% of physicians would dispense a sample that differed from their preferred drug choice.

A study by Tong, et al (Can Fam Phys, 1995), found that 60% of drug reps had used samples themselves or had given them to non-physicians.

A study by Westfall, et al (JAMA, 1997), found that 96% of physicians and staff had taken samples for personal or family use in the preceding year.

The AMA generates \$20 million in annu-

al income by selling detailed personal and professional information on all doctors practicing in the United States to the pharmaceutical industry (NY Times, November 16, 2000)

Spending for prescription drugs in the United States was estimated to be \$111 billion in 1999, a 19% increase over 1998. Spending in the first 10 months of 2000 has surpassed \$100 billion. (IMS Health)

While the price of food has increased at the same rate as inflation (15.5%) and the price of housing has increased only .7% more than inflation (16.2%), the prices of the most commonly used prescription drugs have increased by 30.5%. (USAAction)

Four categories of drugs accounted for 31% of the \$42.7 billion increase in drug costs from 1993 to 1998. These include seven of the 10 drugs most heavily advertised to consumers in 1998. (National Institute for Health Care Management)

The Office of Technology Assessment (Pharmaceutical Costs, Risks, and Rewards, 1993. pp 90-91, 303) estimated that 22.5% of sales is spent on promotion. Therefore, in 2000, with sales expected to surpass \$120 billion, this figure will exceed \$27 billion dollars. According to industry estimates, the pharmaceutical industry spent \$24 billion dollars on R&D in 1999, 20.8% of sales.

[Quoted from *No Free Lunch* website: [www.nofreelunch.org](http://www.nofreelunch.org)]

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Initiated: 1964

17.C  
Original: English

## WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

### Ethical Principles for Medical Research Involving Human Subjects

**ORIGINAL VERSION**

Adopted by the 18th WMA General Assembly  
Helsinki, Finland, June 1964  
and amended by the  
29th WMA General Assembly, Tokyo, Japan, October 1975  
35th WMA General Assembly, Venice, Italy, October 1983  
41st WMA General Assembly, Hong Kong, September 1989  
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996  
and the  
52<sup>nd</sup> WMA General Assembly, Edinburgh, Scotland, October 2000

#### A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must

continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.
9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

## **B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH**

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.
11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.
12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.
14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.



15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.
19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
20. The subjects must be volunteers and informed participants in the research project.
21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.
27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

**C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE**

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.
29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.
30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.



32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.



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## PUBLIC CITIZEN - CONGRESS WATCH

**Public Citizen is a 150,000 member non-profit organization based in Washington, D.C. representing consumer interests through lobbying, litigation, research and public education.**

**Since its founding by Ralph Nader in 1971, Public Citizen has fought for consumer rights in the marketplace, safe and affordable health care, campaign finance reform, fair trade, clean and safe energy sources, and corporate and government accountability. Public Citizen has five divisions and is active in every public forum: Congress, the courts, governmental agencies and the media. Congress Watch is one of the five divisions.**

**We reprint two extracts from a Public Citizen's Congress Watch report dated July 23, 2001 and titled: Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card"; The full version of this very important document, together with appendixes and references, are available at: <http://www.citizen.org/congress/drugs/R&D/scarecard.html>**

### FIRST EXTRACT EXECUTIVE SUMMARY

This new Public Citizen report reveals how major U.S. drug companies and their Washington, D.C. lobby group, the Pharmaceutical Research and Manufacturers of America (PhRMA), have carried out a misleading campaign to scare policy makers and the public. PhRMA's central claim is that the industry needs extraordinary profits to fund expensive, risky and innovative research and development (R&D) for new drugs. If anything is done to moderate prices or profits, R&D will suffer, and, as PhRMA's president recently claimed, "it's going to harm millions of Americans who have life-threatening conditions." But this R&D scare card – or canard – is built on myths, falsehoods and misunderstandings, all of which are made possible by the drug industry's staunch refusal to open its R&D records to congressional investigators or other independent auditors.

Using government studies, company fil-

ings with the U.S. Securities and Exchange Commission and documents obtained via the Freedom of Information Act, Public Citizen's report exposes the industry's R&D claims:

- The drug industry's claim that R&D costs total \$500 million for each new drug (including failures) is highly misleading. Extrapolated from an often-misunderstood 1991 study by economist Joseph DiMasi, the \$500 million figure includes significant expenses that are tax deductible and unrealistic scenarios of risks.
- The actual after-tax cash outlay – or what drug companies really spend on R&D – for each new drug (including failures) according to the DiMasi study is approximately \$110 million. (That's in year 2000 dollars, based on data provided by drug companies.) (See Section I)
- A simpler measure – also derived from data provided by the industry – suggests that after-tax R&D costs ranged from \$57 million to \$71 million for the average new drug brought to market in the 1990s, including failures. (See Section II)
- Industry R&D risks and costs are often significantly reduced by taxpayer-funded research, which has helped launch the most medically important drugs in recent years and many of the best-selling drugs, including all of the top five sellers in one recent year surveyed (1995).
- An internal National Institutes of Health (NIH) document, obtained by Public Citizen through the Freedom of Information Act, shows how crucial taxpayer-funded research is to top-selling drugs. According to the NIH, taxpayer-funded scientists conducted 55 percent of the research projects that led to the discovery and development of the top five selling drugs in 1995. (See Section III)
- The industry fought, and won, a nine-year legal battle to keep congressional investigators from the General Accounting Office from seeing the industry's complete R&D records. (See Section IV) Congress can subpoena the records but has failed to do so. That might owe to the

fact that in 1999-2000 the drug industry spent \$262 million on federal lobbying, campaign contributions and ads for candidates thinly disguised as "issue" ads. (See accompanying report, "The Other Drug War: Big Pharma's 625 Washington Lobbyists")

- Drug industry R&D does not appear to be as risky as companies claim. In every year since 1982, the drug industry has been the most profitable in the United States, according to Fortune magazine's rankings. During this time, the drug industry's returns on revenue (profit as a percent of sales) have averaged about three times the average for all other industries represented in the Fortune 500. It defies logic that R&D investments are highly risky if the industry is consistently so profitable and returns on investments are so high. (See Section V)

- Drug industry R&D is made less risky by the fact that only about 22 percent of the new drugs brought to market in the last two decades were innovative drugs that represented important therapeutic gains over existing drugs. Most were "me-too" drugs, which often replicate existing successful drugs. (See Section VI)

- In addition to receiving research subsidies, the drug industry is lightly taxed, thanks to tax credits. The drug industry's effective tax rate is about 40 percent less than the average for all other industries. (See Section VII)

Drug companies also receive a huge financial incentive for testing the effects of drugs on children. This incentive called pediatric exclusivity, which Congress may reauthorize this year, amounts to \$600 million in additional profits per year for the drug industry – and that's just to get companies to test the safety of several hundred drugs for children. It is estimated that the cost of such tests is less than \$100 million a year. (See Section VIII)

- The drug industry's top priority increasingly is advertising and marketing, more than R&D. Increases in drug industry advertising budgets have averaged almost 40 percent a year since the government relaxed rules on direct-to-consumer advertising in 1997. Moreover, the Fortune 500 drug companies dedicated 30 percent of their revenues to marketing and administration in the year 2000, and just 12 percent to R&D. (See Section X) (...) ►►

## SECOND EXTRACT CONCLUSION AND RECOMMENDATIONS

The prescription drug industry is arguably America's most government-coddled industry. It receives a 20-year monopoly patent on the drugs it develops, permitting companies to charge whatever the market will bear for life-saving drugs. The industry is one of the least taxed in America, yet it has the highest profit margin of all industries – three times the average of all industries. It claims to be a high-risk industry, yet for almost two decades it has topped the profit charts by a factor of two and more recently three. Taxpayers fund significant amounts of the research that results in new drug discoveries, but demand next to nothing in return – not even a simple accounting of our investment. It is time to form a new relationship on behalf of America's consumers between our government and the drug industry.

The financial outlook for the prescription drug industry has never been healthier. In 2000, the 11 largest drug companies netted \$28 billion in profits – a 15 percent increase in their return on revenue over 1999. (See Public Citizen's report at <http://www.citizen.org/congress/drugs/factshts/mostprofitable.htm>). The profits of one drug company, Merck (\$6.8 billion), were larger than the combined profits of all the Fortune 500 companies in each of the following industries: airline, entertainment, metals, food production and hotel/casino/resort industries.

And the picture looks just as rosy, if not rosier, for the future. As Fortune magazine noted in a recent issue, "Never has an industry had brighter long-term prospects...pharma is highly likely to match or exceed the past decade's performance, in which it generated average annual returns of 25 percent. In a queasy economy, that's powerful medicine indeed."

Public Citizen believes that it is essential that America maintain a strong and vibrant prescription drug industry – one that provides healthy but reasonable profits to attract investors. However, this report shows that there is no essential connection between high prices and revenues for the industry and the invention of new medications. The industry has massively overstated the amount it spends inventing new drugs. It devotes much more of the revenue it takes

in to paying dividends to its stockholders and to promoting drugs it has already created than it does to inventing new drugs. It leaves much of the truly pioneering research into deadly diseases to publicly funded researchers at the National Institutes of Health and universities around the world. And the drugs the industry "invents" are more likely to be knock-offs of drugs already on the market than they are to be new cures for a deadly disease.

In light of this situation, Public Citizen makes the following recommendations to Congress:

### A. Drug Price Cost Containment

**1. Medicare cost containment:** As Congress debates enacting Medicare prescription drug coverage there is a deafening silence about giving Medicare the authority to negotiate drug prices as it already negotiates hospital and physician payments. If the Departments of Defense and Veterans' Affairs can negotiate deep price cuts there is no rationale for prohibiting Medicare from doing the same. Yet no major bill proposes such authority because of the power of the drug industry over lawmakers. As recent Congressional Budget Office projections show, given the rising cost of drugs and the budgetary limits placed on a drug benefit, it will be very difficult to construct a benefit that is generous enough along with premiums and cost sharing that are low enough to attract a sufficient number of Medicare beneficiaries to make the program viable. The logical solution is to reduce the cost of drugs. There are different ways to allow for Medicare negotiated prices – the bottom line could be a savings that is 30 percent to 40 percent greater than that anticipated under current Democratic reform proposals using a pharmacy benefit manager model. The Merrill Lynch investment company noted in a 1999 report that such savings would result in a net revenue loss to the drug industry of only 3.3 percent because lower prices would stimulate greater demand.

**2. Reasonable pricing of drugs developed with taxpayer support:** Drug companies should be required to sell drugs that have benefited from taxpayer-funded research at reasonable prices to all, including the Medicare program. Reasonable prices would be determined in a fashion similar to that used in other advanced indus-

trialized countries. Drug companies would be required to submit price applications in which they would propose a price at which they planned to sell their drug along with a justification for that price. The justification would include a listing of the research and development expenses by the company, a detailed accounting of the role of federally-funded research in the development of the drug, and the anticipated therapeutic benefit of the drug. The reasonable price would be set such that the company would receive a healthy but reasonable profit above and beyond its expenses. In determining a reasonable price for a drug, an examination would also be made of the price of drugs in the same therapeutic class in the U.S. and other advanced industrialized countries. The reason that taxpayers fund government research through the National Institutes of Health (NIH) is to develop cures for dread diseases. Clearly, NIH research does little good if consumers cannot afford the drugs that were developed with our tax dollars. This proposal would benefit all those who rely on essential medications, not just Medicare beneficiaries.

**3. Payment based on the value of drugs:** As discussed in this report, much of the research and development and advertising by the drug industry is for the production and marketing of me-too drugs, which represent little or no therapeutic improvement over existing drugs. FDA should require studies of the comparative efficacy and safety of drugs as a condition of their approval. Medicare should not cover new drugs unless there is scientific documentation of a therapeutic advantage over older approved drugs. For drugs that show a genuine therapeutic advance, Medicare would cover the drug and negotiate a fair price based on the new innovation. If Medicare were to do this, then a Medicare drug benefit would not hinder genuine innovation, as the drug industry has asserted, but might act as an inspiration to innovation. In the event that Medicare were unable to create a system of negotiated payments based on a drug's value, then studies of drugs' comparative value could be conducted through the Centers for Education Research and Training (CERT) created under Food and Drug Administration Modernization Act of 1997 (FDAMA). CERT sites are independent, academic centers that given adequate funding could evaluate the comparative value of

drugs. Private payers should use the work of the CERT sites to set their coverage policies for new drugs as a way of controlling costs in the private sector and creating an incentive for innovative research.

## B. Industry Transparency & Preventing Conflicts of Interest

**1. Better tracking of taxpayer developed drugs:** Legislation must be enacted that requires the NIH to maintain a public record detailing the extent of federally-funded support towards the research and development of new drugs. By forcing the NIH to formally track the role of research it funds in the creation of new drugs, the public will be better able to hold the industry accountable for how it uses the research it is given and be able to seek compensation for such public assistance in the form of reasonable prices for drugs.

**2. Require disclosure of the cost of R&D:** Since drug industry claims about the cost of R&D play such a prominent role in its campaign to oppose Medicare drug coverage and Medicare-negotiated drug prices it would be very valuable for the government and private sector to be able to determine how much it costs for the industry to develop new medicines. Currently, only Congress may subpoena drug company financial records to determine what the industry spends on R&D – authority it has not used. The General Accounting Office also should be given such authority in order to determine if the numerous government programs that purchase drugs are being defrauded.

**3. Require disclosure of best prices:** The public debate over what can be done about the high price of prescription drugs for U.S. seniors and other consumers has been stymied by a lack of information about the discounts that the industry offers its most favored domestic and foreign purchasers. Legislation should be enacted that would force the industry to reveal to policy makers the lowest prices it charges to purchasers here and abroad.

**4. Prohibit drug researcher conflicts of interest:** Oftentimes, researchers use non-profit institutions to apply for government research grants, but then enrich themselves by funneling the results of that research to for-profit companies that they control or are employed by. Congress should enact legislation to prevent such abuse of the taxpayer

trust. Or, if Congress is unwilling to prohibit such conflicts of interest, it should require grant recipients to fully disclose them.

## C. Ending Corporate Welfare

**1. End the pediatric incentive for all new drugs:** Pediatric exclusivity is a provision in current law that gives drug companies an additional six months of monopoly marketing protection for testing drugs in children. If this provision is reauthorized this year it will mean \$29 billion in additional revenue for the brand-name drug industry over the next 20 years. This provision should not be reauthorized. Instead, Congress should grant the FDA authority to require that all new drugs likely to be used in children be studied for safety and efficacy in children as a pre-condition of marketing approval. The FDA has estimated the annual cost of conducting those studies if they had been required between 1993 and 1997 at \$80 million.<sup>75</sup> This is a modest cost in exchange for lucrative monopolies granting the rights to market a prescription drug. The amount represents less than one-half-of-one-percent of the \$28 billion in profits earned by the top 11 drug companies in 2000. For more on this go to: <http://www.citizen.org/congress/drugs/pedexclusivityfactsheet.html>.

**2. No patent extensions/no patent abuses:** The Hatch-Waxman Act, which was passed in 1984, has been described as legislation that balanced the public's need for access to lower-priced generic drugs and the brand name drug industry's need for adequate revenues to fund the research and development it uses to invent medications. However, in the years since the Act was passed the drug industry has exploited loopholes in the law to extend their lucrative patents on drugs in ways that were not intended by the Act. One of the loopholes in the law is a provision that prevents a generic from coming to market for 30 months after a lawsuit for patent infringement has been filed against them by a brand name company. The industry exploits this loophole by filing frivolous lawsuits against generics — thus delaying the entry of competing products by at least 30 months. This provision in the Hatch-Waxman Act should be revised so that brand name drug companies can only receive protection from competition if they can prove in a court of law that there is a good reason that a competing generic ►►

## LIST OF ISDB MEMBERS ON THE INTERNET, UPDATED SEPTEMBER 2001

*The following list may not be complete or have errors, please send your details or amendments to [christophe.kopp@wanadoo.fr](mailto:christophe.kopp@wanadoo.fr)*

- Arznei-telegramm (Germany)**  
<http://www.arznei-telegramm.de>
- Australian Prescriber (Australia)**  
<http://www.australianprescriber.com/>
- Belgisch Centrum voor Farmacotherapeutische Informatie (Belgium)**  
<http://www.bcfi.be>
- Boletín Terapéutico Andaluz (Spain)**  
<http://www.easp.es>
- Buttleti d'Informacio Farmacoterapeutica (Spain)**  
<http://www.csbcn.org/public/bif>
- Der Arzneimittelbrief (Germany)**  
<http://www.arneimittelbrief.de/ambstart/starfs.html>
- Dialogo sui Farmaci (Italy)**  
<http://www.dialogosuifarmaci.org>
- Drug and Therapeutics Bulletin (United Kingdom)**  
<http://www.which.net/health/dtb/main.html>
- Drugs Moldova (Moldova)**  
<http://www.aiha.com/english/general/projects/drugs.htm>
- Farmakon (Slovenia)**  
<http://www2.arnes.si/~ljslfd1>
- Focus (Italy)**  
<http://www.sfm.univr.it>
- Geneesmiddelenbrief (Belgium)**  
<http://www.farmaka.be>
- Geneesmiddelenbulletin (the Netherlands)**  
<http://www.geneesmiddelenbulletin.nl>
- Information from Lakemedelsverket (Sweden)**  
<http://www.mpa.se>
- Informazioni sui Farmaci (Italy)**  
<http://www.fcr.re.it/>
- La Lettre du GRAS (Belgium)**  
<http://www.ulb.ac.be/esp/gras/index.html>
- Pharmainformation (Austria)**  
<http://info.uibk.ac.at/c/c5/c515/pharmainfo.html>
- Pharma-Brief (Germany)**  
[http://www.epo.de/bukopharma ►►](http://www.epo.de/bukopharma)

► ought to be kept off of the market. This change is contained in legislation pending before the U.S. House and Senate, the Greater Access to Affordable Pharmaceuticals Act, Schumer-McCain/Brown-Emerson, S. 812/H.R.1862.

#### **D. Comparative Drug Information**

**1. Require the FDA to estimate the therapeutic value of new drugs:** In order for the public and private sectors to be better equipped to negotiate lower drug prices, better information is needed about whether new products may offer a therapeutic advantage over older drugs or are simply me-too drugs. This would be similar to the system used by the FDA prior to 1992 in which it distinguished between drugs that represented an “important therapeutic gain, a “modest therapeutic gain,” and “little or no therapeutic gain.”

Congress should require the FDA or else establish a private entity to study the comparative value of all prescription drugs so that consumers, payers, and doctors can be better informed. If funding for the Centers for Education, Research and Training established under FDAMA were increased, they could do this research. As a condition of federal support, academic medical centers could be required to use this unbiased information in educating medical students and in continuing medical education so that doctors can make distinctions between “me-too” and breakthrough drugs in their prescribing decisions. Also, such information would be made available to medical insurance payers so that they could make better decisions about which drugs to cover.

#### **E. Regulate Drug Company Advertising and Promotion**

**1. Require FDA to promulgate regulations for direct-to-consumer (DTC) advertising:**

As this report shows, drug company advertising to consumers plays a role in rising prescription drug costs. But currently there is limited FDA authority to regulate such advertising. Congress should require the FDA to issue regulations concerning DTC advertising by a date certain. These regulations should require that drug companies provide consumers with scientifically accurate, useful, comparative information about the value of drugs in their advertisements and in the packaging of the drugs they

manufacture.

**2. Assure adequate FDA funding to monitor both professional and DTC advertising:**

The FDA office charged with overseeing drug advertising, the Division of Drug Marketing Advertising and Communication (DDMAC), is woefully understaffed. While the dollar value of DTC advertising and promotion has more than tripled from \$791 million in 1996 to \$2.5 billion in 2000, and other advertising, to professionals, also increased, the number of FDA staff assigned to review and investigate all prescription drug advertising during this same period has increased from 11 to only 14. Clearly, in order for FDA to protect consumers from misleading claims in advertisements by the drug industry that help to fuel double-digit spending increases, additional staff for DDMAC is essential.

**3. Strengthen FDA enforcement:**

To give FDA stronger enforcement powers, Congress should give the agency the authority to level civil monetary fines for misleading drug advertising. The FDA has asked for such authority in the past. (See *American Journal of Law and Medicine*, 1999, p. 149.).

► **Pharma-Kritik (Switzerland)**  
<http://www.infomed.org/pharma-kritik-e/>

**Prescriber Update (New Zealand)**  
<http://www.medsafe.govt.nz/Profs/Puarticles.htm>

**PRN Bulletin (Malaysia)**  
<http://prn.usm.my/bulletin/>

**Rational Drug Bulletin (India)**  
<http://www.healthlibrary.com/reading/rdb/index.htm>

**Therapeutic Guidelines (Australia)**  
<http://www.tg.com.au>

**Therapeutic Initiative (Canada)**  
<http://www.interchange.ubc.ca/jauca>

**Worst Pills Best Pills (United States)**  
<http://www.citizen.org/hrg/NEWSLETTERS/pillnews.htm>