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Content

Pharmaco-Economic Society Warsaw, October 17th, 2006

To Honorable Ministers of Health in the EU countries

Re innovative medicines and health for all

Dear Sirs,

Political essence of health economics is not only the evaluation of medical technologies and medicines but a proper economic selection of existing medicines in order to give health to all.

Pharmaceutical industries do their best to convince the European Commission and the particular governments that new patented drugs lead to added value in the medicinal sector, are crucial to Europe, should be recognized, and promoted (reimbursed from public funds).

We notice that your delegates to the Working Group on the Pharmaceutical Forum on "Pricing and Reimbursement" do not distinguish valuable innovations from invaluable ones. There is a tendency of accepting the corporate idea that all (or almost all) new patented medicinal products are innovations deserving recognition and public funds.

We feel it is our duty to warn you that most new medicinal products are pseudo-innovations. They are very often "innovations" of inferior effectiveness.

Scientists invent from time to time a new valuable medicine, e.g.

1953 Chlorpromazine (Largactil)
1957 Chlorothiazide (Diuril), 1962 Hydrochlorothiazide (Esidrex)
1959 Chlordiazepoxide (Librium), 1963 Diazepam (Valium)
1964 Propranolol (Inderal)
1967 Glibenclamide (Daonil)
1968 Salbutamol (Ventolin)
1968 Nifedipine (Adalat)
1974 Cimetidine (Tagamet), 1978 Ranitidine (Zantac)
1977 Captopril (Capoten), 1980 Enalapril (Vasotec)
1979 Omeprazol (Losec)
1980 Lovastatin (Mevacor)

Every drug improving health is well accepted by doctors and patients. Every new drug is patented, monopolistic, very expensive. Every new successful drug makes the company-producer a multimillionaire.

Other companies are jealous. They order their chemists to synthesize similar molecules; pharmacists call them "me-too drugs". A similar molecule works therapeutically like the ancestor. Sometimes better, mostly - worse. Each one me-too drug is promoted and sold at the price equally high or higher to the ancestor's price. Lower price would impress doctors and consumers that the product is worse.

Parke Davis/Warner Lambert/to-day Pfizer with petty expense on R&D makes atorvastatin, me-too lovastatin, and sells for USD 12 billions (milliards) a year.

It makes no difference for the payer as long as lovastatin and atorvastatin are protected by patents. However atorvastatin invented 11 years later than lovastatin is unnecessarily for 11 years ruining your national health services, if you reimbourse its price.

In Germany atorvastatin pays euro 1,03/DDD (10 mg). We are able to flood the whole country with lovastatin at euro 0,15/DDD (30 mg). German Krankenkassen reimbourse 475,3 milions DDD atorvastatin a year. They overpay euro 418 mln [475,3 · (1,03 - 0,15)].

Most medicinal products on sale are me-too drugs. Excellent chlorpromazine (Largactil) was distorted 41 times. Famous propranolol (Inderal) was followed by 27 me-too molecules. Benzodiazepines similar to chlordiazepoxid or diazepam were 36. Captopril, enalapril et cetera are a family of 16 members.

Real innovations requiring huge money on the R&D are few.

Dear Sirs, do not allow to consider that pseudoinnovations are really innovations. They are not. Do not accept compulsory reimboursement of all new patented expensive drugs entering the market.

It would cost you enormous money and deprive your population of numerous medicines (health money is always short).

It would slow down the pharmaco-medical progress. The industry granted enormous money for peanut is not warranted for working hard.

Do accept only reimboursement of medicines serving best your country.

President
Dr Tadeusz J. Szuba

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Tadeusz J. Szuba

Deception in the pharmaceutical innovativeness

Big pharmaceutical companies emphasize their – purportedly enormous – contribution to inventing new drugs. Happiness of the mankind is supposed to be the result of their activities. These companies do not only care about their public relations and reputation. What is at stake here is consent for enormous profits (many billions of euros) made by them.

This issue requires careful examination because it is becoming dangerous. An association of pharmaceutical companies is exerting pressure on the European Commission to apply a suitable directive and force EU member countries to reimburse automatically the registered innovative drugs. The association argues that if we want to have the "health" progress in Europe, we must support the innovative drugs' market.

The European Federation of monopolistic (monopolistic – because they commercialize products that no other companies are permitted to manufacture or sell because of patents and brands) Pharmaceutical Industries and Associations [EFPIA] employs highly qualified economists to present achievements of the industry when it comes to innovativeness. The following is an example of the scientific propaganda prepared by the Office of Health Economics [OHE], and widely distributed in Brussels and EU countries (1):

– "Innovation should not be considered in terms of "black and white" or "it is – it is not",

– The approach that tries to categorize new drugs as breakthroughs and as ones that bring better effects is misleading. Innovation should be seen as continuum,

– The consumer is the final judge when it comes to the product value and degree of its innovativeness; in pharmacology, the consumers do not usually pay and it is the third party who does this, so the payer should take the patients' wishes into consideration when deciding about drug reimbursing."

According to this, the new drug may not bring better effects but the high price must be paid anyway because the consumer (usually an ignorant person) demands this! This kind of disinformation propaganda takes 34 pages of a text with a wide "scientific" bibliography.

In Brussels, the most important commissionaires (ministers) come from the most developed countries – Germany, the United Kingdom, France – which greatly profit from pharmaceutical companies. So the commissionaires show a natural tendency to support these companies.

Health ministers from 25 EU member countries do not all posses economic and pharmaceutical knowledge and being unaware of the danger might accept the obligation to reimburse new drugs from public funds.

That is why, for the sake of Europe and the world, let's try to propagate the truth about drugs, pharmaceutical innovations, prices and reimbursement.

Why are the producers so keen on forcing sales of the innovative new medicines with the aid of governments? It is because the companies are legally able to charge for those innovative drugs (which are patented i.e. monopolistic) any desired price. Of course, a very high price. Until now, European governments have decided on reimbursing drugs at their own discretion. They were free to decline the reimbursement of new drugs when they were not better but more expensive than older ones.

The independent decisions of governments have not made pharmaceutical companies happy. That is why they are so deeply and politically involved in Brussels. For that reason, let us try to make an effort of saying the truth about innovativeness.

The analysis of innovativeness must be based on hard facts, on the evaluation of new products entering the market. It might be possible to review modernization of the drug assortment in particular countries, that is, the entire world. However, this would take a long time and would be hard to read. So this study is limited to one country – Germany – as a representative for the pharmaceutical progress (in Germany all new drugs were registered and not just the ones that were invented in Germany).

In addition, this study is limited to the medicines that were modestly accepted by health services (drugs that were not prescribed 10,000 times during one year in the whole country – were not included in the study). Instead, the review takes into consideration a long period of time – 12 years (1991-2002). Official reports of the German Health Care Funds were used as a source of data (2).

The detailed data was included in Annex 1 in which new drugs in the WHO ATC order were listed together with a commentary about inventiveness of their creator and the category of the contributed progress.

On the list, the highest grade is awarded to a drug not because it provides treatment (every drug does that) but because it is original and innovative and contributes to the progress in pharmacology.

During the tested period there were 190 new medicines. Out of them, only 15 were identified as those that contributed to the advancement (8%):

Ondansetron – used to prevent vomiting and making chemotherapy possible in oncology,

Repaglinide – a drug that lowers the amount of sugar in blood and is not a modification of the already known structures,

Losartan – used to treat high blood pressure and is called agiotensin II receptor antagonist. Although it is not more effective than excellent ACE inhibitors, it still constitutes a valuable alternative,

Raloxifene – an estrogen reception modulator, a completely original drug,

Finasteride – an inventive testosterone metabolism inhibitor, helpful in treating prostate,

Ribavirin – an antiviral medication, it is a nucleoside structure similar to aciclovir and others but more effective,

Lamivudine – the first, quite effective nucleoside reverse transcriptase inhibitor (used in treating AIDS,)

Nevirapine – reverse transcriptase inhibitor but not a nucleoside structure,

Imatinib – an original and quite effective drug used in oncology,

Glatiramer – an immuno-modulator, different and better than those already on the market,

Etanercept – a selective immuno-inhibitor, clearly useful,

Sumatriptan – the first selective agonist of serotonine, effective against a migraine attack,

Risperidon – effective antipsychotic with an original chemical structure,

Montelukast – a very inventive chemical structure, helpful in preventing asthma symptoms,

Dorzolamide – a carbonic anhydrase inhibitor modeled after acetazolamide but evidently better helpful in treating glaucoma.

Over 12 years, the pharmaceutical industry launched into the pharmaceutical market only 15 new drugs worth any decent payment. There were also about 30 drugs not very original ones but which contributed to the progress and deserved a nice fee. Here are a few examples:

Amlodipine – almost zero of invention, new congener of the old drug – nifedipine but acting better,

Azithromycin – a new antibiotic made from erithromycine, a known macrolide structure, but effective,

Carvedilol – an easy to invent beta-blocking agent, like other adrenergic blockers, has also poor alpha blocking properties, appeared good for some patients,

Olanzapine – a simple congener (me-too) of clozapine but much more effective,

Tamsulosine – an alpha blocking structure, small "invention", costly R&D was needless, luckily, it is effective in helping patients with a benign prostate hypertrophy,

A decisive majority of the new registrations 190 – (12 + 30) = 148 include the "me-too" drugs – modifications of the already existing ones – that were invented not for the sake of progress but money. Only money. And without any great effort.

Taking advantage of the fact that physicians do not have sufficient knowledge of chemistry and are unable to differentiate between an original innovation and its modification and the consumers lack science of pharmacological commodities, pharmaceutical companies beguile the world with their "enormous" contributions, which, in fact, do not exist. The innovative achievements of the pharmaceutical industry are a monstrous deception.

Even the true aforementioned inventions are not as a rule made by the pharmaceutical industry but outside of it – in universities and scientific institutes financed by public funds. This truth is carefully kept hidden but sometimes it comes out. For example, the super invention – imatinib – was not only made outside of the industry but the industry itself made a lot of effort to sabotage its production. The case was described by an US expert on pharmaceutical and medical progress in her book (3).

Most of the supposed inventions are only commissioned by the pharmaceutical companies and are made in many different places. The mechanism of this innovativeness is as follows:

Somebody made a perfect drug, for example, propranolol – a beta-blocker, which revolutionized cardiology. Its inventor was not a well-known scientist. He worked for a small pharmaceutical unit (Pharma Division in the ICI, later called Zeneca). Propranolol was a good medicine, which became a hit. A lot of people have to regulate their heart function and lower their blood pressure. The sales of propranolol (Inderal) were record high. So were the profits. A patent protects the product, so of course, no other company but the one that patented the drug might produce and sell it.

So, what do other companies do in such a case? They commission

chemists to produce molecules that are very similar to propranolol but at the same time different enough so the ICI patent might be evaded and the companies might obtain the patent for their new drug.

The "me-too" medicines, chemical congeners, are made with almost no effort, while their price is the same as that of a brand Inderal (propranolol). In medicine, products do not compete when it comes to their prices because doctors and consumers have experience from other markets, such as textiles or food products, where cheaper means inferior quality. That is why, in pharma-business, the competition is limited to a promotion that "my product is super." There might be a lot of such super products – five, ten, twenty or more. In case of propranolol, there are 28 of them: propranolol, oxprenolol, pindolol, alprenolol, timolol, sotalol, nadolol, mepindolol, carteolol, tertatolol, bopindolol, bupranolol, penbutolol, clovanolol, practolol, metoprolol, acenolol, acebutolol, betaxolol, bevantolol, bisoprolol, celiprolol, epanolol, S-atenolol, nebivolol, talinolol, labetalol and carvedilol.

Obviously, some of them are better and some are worse. Currently, doctors throughout the world most often use metoprolol, which might suggest that it is the best or at least one of the best. However, this does not stop pharmaceutical companies from saying that their drugs are the best. In this situation, for example, the main expert of the Polish reimbursement commission, quoting the opinion of the European Cardiology Society, demands that nebivolol is included in the list of the reimbursed drugs. Supposedly it is used routinely in cases of heart failure. (4). The medical expert is not at all interested in the fact that nebivolol costs PLN 2.814/DDD (5 mg), while metoprolol costs PLN 0.378/DDD (150 mg) – the difference being 7.5 times. Look at the list of prices (5). With the consumption of the "olol" drugs in Poland reaching 1 billion DDD annually, this difference in the price translates into an increase of the health care costs by close to PLN 2.5 billion: 1.000.000.000 x (2.814 – 0.378) = 2.436.000.000.

Let's keep in mind that Poland's governmental funds amount to PLN 6.3 billion for purchasing all medicines. The reckless use of nebivolol instead of metoprolol would unnecessarily eat up to 40% of all health care funds allocated to treat all diseases in all patients!

We may cope with the polish "expert", even a professor of medicine. However, we would not be able to manage financing drugs if the European Commission told us to reimburse all innovations.

The commissionaires in Brussels are dangerous because they are not pharmacists and do not know the secret of managing drugs. A very good medicine that was invented "yesterday" (propranolol in 1964, atenolol in 1970, metoprolol in 1971, bisoprolol in 1978) is not protected by a patent, is produced competitively and that is why, it is cheap. A similar drug, which might be even of inferior quality, but has been invented "today", is protected by a valid patent and monopolistic so it is very expensive.

The flood of the "-olol" innovations following the propranolol success

is nothing extraordinary. This kind of "innovativeness" has been practiced everywhere forever.

When chlordiazepoxid (Librium) and diazepam (Valium) became greatly successful, an avalanche of benzodiazepins, have engulfed the market, including anxiolitics: medazepam, oxazepam, clorazepam, lorazepam, adinazolam, bromazepam, clobazam, ketazolam, prazepam, alprazolam, halazepam, pinazepam, camazepam, nordazepam, fludiazepam, loflazepam, etizolam, clotiazepam, cloxozolam, tofisopam and hypnotics: flurazepam, nitrazepam, flunitrazepam, estazolam, triazolam, lormetazepam, temazepam, midazolam, brotizolam, quazepam, loprozolam, doxefazepam, cinolazepam. In total, there were 36 "inventions" made for money and not health reasons because it is common knowledge that benzodiazepins have been abused for years and it would be better to discourage the public from taking them rather than to promote their use.

Undoubtedly, neuroleptic chlorpromazine (Largactil) was even a bigger success. It not only helped but also cured patients. It deserved the profits running into billions. But it also liberated "inventiveness" of the companies that call themselves innovative: they made 41 drugs similar to chlorpromazine.

The profits made by a useful invention to treat asthma – salbutamol (Ventolin) – provoked a whole flood of analogical adrenergic medicines, including: fenoterol, terbutaline, hexoprenaline, pirbuterol, carbuterol, tulobuterol, salmeterol, formoterol, clenbuterol, reproterol, procaterol, bitolterol and others. The biggest profits were made from long-acting salmeterol, which it turned out to be dangerous (causing death) according to the Food and Drug Administration [FDA] in USA.

The cimetidine (Tagamet), which made billions in profits and was a crucial invention to treat gastric hyperacidity and ulcers, was followed by an appearance of a whole series of similar inventions, including: ranitidine, famotidine, nizatidine, nieperotidine, roxatidine, lafutidine. Satisfactorily, the "me-too" ranitidine turned out to be better than cimetidine, which makes us not dismiss all "me-too" drugs.

Surprisingly, only a few congeners appeared after the invention of omeprazol, a proton pump inhibitor. They included: pantoprazol, lansoprazol, rabeprazol and finally esomeprazol.

There are 13 sulfonylureas, anti-diabetic agents, on the world market, which were modeled after glibenclamide.

The pseudo-inventiveness found an easy way out in the field of the small-molecule heparin drugs. Here, not even the effort of conducting a synthesis was required. It was enough to break up into parts a molecule of heparin, which had been on the market for a few dozen of years. The idea was good, so many wanted to make money out of it; as a result, we ended up with: enoxaparin, nadroparin, parnaparin, reviparin, dalteparin, tinzaparin, sulodexid, bemiparin, certoparin and antithrombine III, using a

different methods of degradation. Of course, users should believe that each "-parin" is an invention deserving a high price.

Currently, there are, in the world, only 10 diuretic "-thiazid" drugs, which were modeled after chlorothiazid and hydrochlorothiazid. Many of them have already gone "bankrupt."

There are 15 calcium blockers, only those with the dihydropirydine structure and modeled after nifedipine.

There are 16 ACE inhibitors, the so-called "-pril" drugs, which imitate: captopril and enalapril, lowering blood pressure.

There are only eight newer "sartan" drugs, which are similar to "pril" drugs in cardiologic terms.

At the present time, the highest spending is generated by lipid modifying agents from the statin group. They are modifications of lovastatin. There have already been made seven of such drugs but one of them (cerivastatin) was withdrawn from the market as it caused rhabdomyolysis (a severe muscle toxicity).

The biggest orgy of inventiveness from the same mould took place in a group of antibiotics belonging to cefalosporins.

The field of the half-synthetic penicillin drugs was equally fertile.

Joyful inventiveness also spread into anti-mycosis agents with imidazol (and triazol) structure.

The industry was also very generous with hormones. It was especially prolific in "inventing" similar anti-inflammatory corticosteroids – either systemic or dermatological ones. There are dozens of them but the majority is unnecessary.

All the above listed examples prove the thesis that the innovativeness of the pharmaceutical industry is to a great extent illusionary, egoistic (for profit) and not humanitarian (for health).

Somebody might say: let's allow reimbursing all new drugs and people on their own will choose the best and cheapest ones. But patients are as thick as two short planks while doctors who do not pay for drugs are not interested in their prices. On the other hand, producers of expensive drugs can well afford an aggressive promotion, which misleads doctors and pushes out cheap and good medicines from the market. The producers were even able to create persuasive science, according to which, for example, expensive perindopril is cheaper than cheap enalapril. They even called this science "Pharmacoeconomics."

A pharmaceutical "innovative" company does not only push out perfect and cheap drugs produced by generic companies. It often pushes out of the market its own perfect drug as soon as it loses its patent protection.

At the present time, the case of esomeprazol – omeprazol gives an excellent example of such conduct. Being aware that the patent protection of omeprazol (Losec), which brought billions in profit annually, was running out, the company "invented" esomeprazol (Nexium). It is chemically

identical to omeprazol, has the same properties that curb secretion of the hydrochloric acid and is used to treat ulcers. Esomeprazol is simply an isomer of omeprazol. The company was successful in obtaining a patent for it and it will be able to sell it in a monopolistic and expensive manner for the next 20 years without any competition.

A different company cut short the career of its own, old and perfect drug, ticlopidine, used to prevent platelets from clustering, and introduced into the market a new product – clopidogrel, which is both chemically and pharmacologically similar. Due to its patent monopoly, the company continues to make a profit of billions from selling clopidogrel.

The pharmaceutical industry invents new drugs not for health reasons but to obtain patents and monopolistic position as well as to sell drugs at very high prices.

In rich countries such as the USA, promotion of new drugs is very effective. Esomeprazol is being sold in numbers equaling the old sales of omeprazol. In poor countries, it is not the case. People have no money. That is why pharmaceutical companies exert pressure on governments of such countries to reimburse these pseudo-innovations.

Obviously, pharmaceutical companies cannot tell Brussels directly: "Oblige EU member countries to reimburse expensive esomeprazol or clopidogrel, when there are much cheaper omeprazol and ticlopidine." Instead, these companies might demand protection for innovativeness in rather general terms. Their major argument being the supposedly great good for humanity brought by innovations and their supposedly enormous costs paid at the altar of R&D.

Lies are being spread – in all possible publications and magazines, not only medical and pharmaceutical ones, but also popular ones (such as Newsweek) – that in order to create a new drug, 10,000 synthesis of new chemical compounds must be conducted, out of which something useful might be selected. In total, a search for a new drug together with its clinical trials costs almost one billion US dollars.

These pharmaceutical companies do not appreciate the intelligence of listeners and readers. Annex 1 shows that the decisive majority of the new drugs belong to congeners and chemical modifications that were made to evade patents of other drugs, which seldom were inferior in comparison to their new versions. In order to create a "me-too" drug, there is no need to conduct 10,000 syntheses – just one is often enough.

In addition, the declared costs of producing a new drug are also grossly inflated. The production of a congener is cheap. We know this well from our own Polish experience. We used to make very cheaply very good "me-too" drugs such as proxibarbal (Ipronal), gapicomine (Bicordin) and others.

However, one must not exaggerate when criticizing pharmaceutical innovations. It does happen that a new congener is better than its old model. It might be a congener that is very simple to produce. For example, when a great diuretic innovation – chlorothiazid – appeared on the market and its producer stared making a fabulous profit, hydrochlorothiazid was very quickly manufactured. The difference between the two was just one atom of hydrogen. But it proved to be more effective and contributed to the therapeutic advancement.

Our intention is not to condemn every last one of the "me-too" drugs but to learn the truth about them and to hinder the deception. One should learn not only about medicine but also about its business aspect. Billions can be made or lost while uncritically using congeners, which are basically new – so protected by patents, monopolistic and expensive while their older prototypes are being made by many competing companies and are thus cheap. The price difference is not a question of 5, 10 or 20%; it is often 200, 500 or 1000%. In poor countries, this simply means that health or even lives of as many as thousands of people will not be saved, if money is wasted on unnecessary and expensive drugs.

The quantity of losses or gains depends on the size of a country (the size of its population) and its governmental drug policy.

It is worth knowing that the world spends the biggest amount of money not on original and real inventions (omeprazol, captopril/ enalapril, imatinib etc.), but on the "me-too" drugs. Currently, the biggest amount of money is spent on atorvastatin, sold to the tune of USD 13 billion annually. It brings to its producers the unjust profits of probably USD 10 billion while its inventing and manufacturing costs not much. It is a modification of a real innovation – lovastatin.

Annex 2 presents 20 of the biggest moneymaking drugs in the world with the commentary on their innovativeness. Great many of these drugs were incredibly easy and simple to invent – they are plain modifications of the earlier inventions and they are not necessarily better than their predecessors. For example, in the opinion of the authoritative National Institute for Clinical Excellence [NICE] from the UK, atorvastatin is not better than lovastatin, simvastatin or other statins. The UK National Health Service is supposed to choose the cheapest one.

Similarly, there is no uncommitted clinical literature convincing us that the afore-mentioned clopidogrel is better than ticlopidine, which is currently much cheaper.

The third biggest moneymaking drug, which contains salmeterol is raising increasing reservations regarding its quality – USD 5.5 billion are spent on it but it has caused some deaths.

What is important to remember is the fact that out of 20 biggest drugs in the world, a dozen or so are simple congeners, modeled after the earlier and true inventions.

If the industry that proudly calls itself innovative states that a new drug is a result of searching for 10,000 molecules and costs 500, 750 million or one billion USD dollars, it is simply lying.

The pharmaceutical industry has undoubtedly achieved and contributed much. Efforts of scientists and their achievements might be utilized thanks to the industry. The world should eagerly pay billions of euros for new inventions that contribute to advancement (please, look Annex 1, category A). The world should not stint on paying for new drugs that are not possibly very inventive but noticeably better (please, look Annex 1, category B). But the world should not automatically pay high prices for all new drugs just because they have patents but do not contribute anything to advancement or even push it back (please, look Annex 1, category C). The majority of inventions belong to category C.

Concurrently with the useful activities, the pharmaceutical industry is acting dishonestly. The industry takes advantage of the consumers' (as well as politicians', journalists' and doctors') lack of knowledge. It exploits the patent system to intensify pseudo innovations for profit. Pseudo innovations may be sold at very high price like the real innovations. Of course, the process must be accompanied by aggressive promoting, as well inspiring, writing and publishing of favorable scientific dissertations that mislead millions of doctors throughout the world.

Governments should decisively stand up to this practice. In their national drug policy, they should favor reimbursement from public funds only those drugs that are the best and the cheapest. Governments should not give in to the pressure exerted by the industry and its financially- involved allies and pay for more expensive but not better drugs.

A system of reaching the impartial truth should be prepared. Clinical doctors paid by pharmaceutical companies write about advantages of new drugs. They do this based on clinical trials, most often conducted prior to registration, so with a small number of cured patients. Meanwhile the range of benefits (or their lack) of a new drug comes out when it is widely used. To make the matters worse, even the subsequent opinions of doctors might be questionable because pharmaceutical companies try to help them write these reviews.

Experience teaches us that a new drug that contributes to therapeutic advancement becomes quickly successful on the market – even when it is not aggressively advertised. Many valuable new drugs were commercialized by small and relatively poor companies (e.g. propranolol – ICI, cimetidine – SKF, omeprazol – Astra). They could not spend billions on promotion. Millions of regular doctors, who are generally raised on Hippocratic oath and not corrupted, are the judges deciding what is good.

That is why the decisions about reimbursement should be based on market data and not based on clinical data. Of course, market data must be interpreted with caution. Sales of drugs do not only depend on their benefits but also promotion, which is more effective when a bigger company employing a high number of sales representatives offers the drug. For example, we know that all statins are equally good. We also know that it is atorvastatin that is sold in the highest amounts, even though it is not better than any other statin. However, it is promoted and sold by powerful Pfizer (by the way, atorvastatin was not even invented by Pfizer). Based on this knowledge, the decisionmakers would not have to reimburse of atorvastatin, if it were unreasonably expensive.

A fair national policy is necessary for the good of the public. Wasting public money allotted to buying drugs will deteriorate public access to drugs, will make proper health care impossible and increase death rates.

The conclusions from this study seem to confirm the earlier reflections (6) (7).

Such a policy will also benefit the pharmaceutical industry. If we make it harder for the industry to profit immensely from pseudo-inventions, we will create stronger stimuli for the industry to come up with true inventions.

Activities of governments aimed at protecting their citizens against predatory activities of pharmaceutical companies will no longer be necessary when the world understands that it is the patent system and not the industry that is the source of evil. The patent system for medicines must be reformed but it is another story.

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Annex 1

New drugs in Germany 1991-2002 without the small items (fewer than 10,000 prescriptions)

Number	ATC code	International name	Scientific inventiveness	Year of registration	Category
1.	A02BC	Lansoprazole	me-too Omeprazole	1993	C
2.	A02BC	Pantoprazole	me-too Omeprazole	1994	C
3.	A02BC	Rabeprazole	me-too Omeprazole	1998	C
4.	A02BC	Esomeprazole	isomer of Omeprazole	2000	C
5.	A04AA	**Ondansetron**	true invention	1991	A
6.	A04AA	Tropisetron	me-too Ondansetron	1993	C
7.	A10A	Insulin aspart	modification of insulin	1999	B/C
8.	A10A	Insulin glargin	modification of insulin	2000	B/C
9.	A10A	Insulin lispro	modification of insulin	1996	B/C
10.	A10BB	Glimepiride	me-too Glibenclamide	1996	C
11.	A10BF	Miglitol	me-too Acarbose	1998	C
12.	A10BG	Rosiglitazone	me-too Troglitazone (just withdrawn)	2000	A/D
13.	A10BG	Pioglitazone	me-too Troglitazone (just withdrawn)	2000	A/D
14.	A10BX	**Repaglinide**	true invention	1998	A
15.	A10BX	Nateglinide	me-too Repaglinide	2001	C
16.	B01AB	Reviparin	degradeted heparin	1993	C
17.	B01AB	Tinzaparin	degradeted heparin	1993	C
18.	B01AC	Clopidogrel	me-too Ticlopidine	1998	B
19.	B03XA	Darbepoetin alfa	me-too Erythropoetin	2001	B
20.	C02AC	Moxonidine	me-too Clonidine	1991	C
21.	C02CA	Bunazosin	me-too Prazosin	1994	C
22.	C03CA	Torasemide	me-too Furosemide	1992	C
23.	C07AB	Nebivolol	me-too Metoprolol	1997	C
24.	C07AG	Carvedilol	me-too Labetalol	1991	B
25.	C08CA	Felodipine	me-too Nifedipine	1991	C
26.	C08CA	Nilvadipine	me-too Nifedipine	1992	C
27.	C08CA	Amlodipine	me-too Nifedipine	1994	B
28.	C08CA	Lacidipine	me-too Nifedipine	1998	C
29.	C08CA	Lercanidipine	me-too Nifedipine	2000	C
30.	C09AA	Quinapril	me-too Captopril/Enalapril	1991	C
31.	C09AA	Fosinopril	me-too Captopril/Enalapril	1992	C
32.	C09AA	Benazepril	me-too Captopril/Enalapril	1993	C
33.	C09AA	Trandolapril	me-too Captopril/Enalapril	1993	C
34.	C09AA	Spirapril	me-too Captopril/Enalapril	1997	C
35.	C09AA	Moexipril	me-too Captopril/Enalapril	1997	C
36.	C09AA	Imidapril	me-too Captopril/Enalapril	1999	C
37.	C09AA	Cilazapril	me-too Captopril/Enalapril	1992	C
38.	C09CA	**Losartan**	true invention with little advancement	1995	B
39.	C09CA	Valsartan	me-too Losartan	1996	C
40.	C09CA	Candesartan	me-too Losartan	1997	C
41.	C09CA	Irbesartan	me-too Losartan	1997	B
42.	C09CA	Eprosartan	me-too Losartan	1997	C
43.	C09CA	Telmisartan	me-too Losartan	1999	C
44.	C09CA	Olmesartan	me-too Losartan	2002	C
45.	C10AA	Pravastatin	me-too Lovastatin/Simvastatin	1991	C
46.	C10AA	Fluvastatin	me-too Lovastatin/Simvastatin	1994	C
47.	C10AA	Atorvastatin	me-too Lovastatin/Simvastatin	1997	C
48.	C10AA	Cerivastatin	me-too Lovastatin/Simvastatin (withdrawn)	1997	C
49.	D01AC	Fenticonazole	me-too Miconazole	1991	C
50.	D01AC	Sertaconazole	me-too Miconazole	1995	C
51.	D01AE	Amorolfine	–	1992	C
52.	D01BA	Terbinafine	–	1992	C
53.	D05AX	Calcipotriol	me-too vitamin D_3	1992	B
54.	D05AX	Tacalcitol	me-too vitamin D_3	1996	C
55.	D05BB	Acitretin	me-too Tretinoin	1992	C
56.	D05BX	Fumaric acid alkil ester	–	1994	C
57.	D07AC	Methylprednisolone aceponate	Methylprednisolone ester	1994	C
58.	D10AD	Adapalene	me-too Tretinoin	1996	C
59.	D10AX	Azelaic acid	–	1991	C
60.	D11AX	Pimecrolimus	me-too Tacrolimus	2002	C
61.	G02CB	Metergoline	me-too Bromocriptine	1992	C
62.	G03DC	Tibolone	me-too Norethisterone	1999	C
63.	G03FA	Drospirenone+Estrogen	me-too Norethisterone	2000	C
64.	G03GA	Follitropin alfa	me-too Choriogonadotropin	1996	C
65.	G03GA	Follitropin beta	me-too Choriogonadotropin	1996	C
66.	G03GA	Choriongonadotropin alfa	me-too Choriogonadotropin	2001	A/C
67.	G03XC	**Raloxifene**	true invention	1998	B
68.	G04BD	Tolterodine	–	1998	C/D
69.	G04CA	Alfuzosine	me-too Prazosine	1995	C
70.	G04CA	Tamsulosine	me-too Prazosine	1996	B
71.	G04CB	**Finasteride**	true invention	1994	B
72.	H02AB	Rimexolone	me-too Prednisone	1999	C
73.	J01DC	Loracarbef	semisynthetic cefalosporin	1993	C
74.	J01DD	Cefixim	semisynthetic cefalosporin	1991	B
75.	J01DD	Cefpodoxim	semisynthetic cefalosporin	1991	B
76.	J01DD	Ceftibuten	semisynthetic cefalosporin	1993	C
77.	J01DD	Cefetamet	semisynthetic cefalosporin	1994	C
78.	J01FA	Clarithromycin	semisynthetic erytromycin	1991	B
79.	J01FA	Azithromycin	semisynthetic erytromycin	1993	B
80.	J01FA	Telithromycin	semisynthetic erytromycin	2001	B
81.	J01MA	Fleroxacin	me-too Ofloxacin	1995	C
82.	J01MA	Levofloxacin	me-too Ofloxacin	1998	C
83.	J01MA	Moxifloxacin	me-too Ofloxacin	1999	C
84.	J01MA	Gatifloxacin	me-too Ofloxacin	2001	C
85.	J02AC	Itraconazole	me-too Fluconazole	1991	C
86.	J05AB	**Ribavirin**	invention not original but opportune	1992	B
87.	J05AB	Penciclovir	Vectavir® withdrawn	1997	C
88.	J05AE	Indinavir	me-too Saquinavir	1996	C
89.	J05AE	Nelfinavir	me-too Saquinavir	1998	C
90.	J05AE	Lopinavir	me-too Saquinavir	2001	C
91.	J05AF	Didanosine	me-too Lamivudine	1992	C
92.	J05AF	Stavudine	me-too Lamivudine	1996	C
93.	J05AF	**Lamivudine**	true invention	1996	B
94.	J05AF	Abacavir	me-too Lamivudine	1999	C
95.	J05AF	Tenofovir disoproxil	me-too Lamivudine	2002	A
96.	J05AG	**Nevirapine**	true invention	1998	A
97.	J05AG	Efavirenz	me-too Nevirapine	1999	B
98.	J05AH	Zanamivir	me-too Aciclovir	1999	C
99.	L01BC	Capecitabine	me-too Cytarabine/Gemcitabine	2001	B
100.	L01BC	Gemcitabine	me-too Citarabine	1996	C
101.	L01XC	Trastuzumab	•	2000	A/D
102.	L01XX	**Imatinib**	true invention	2001	A
103.	L02BB	Bicalutamide	me-too Flutamide	1996	B
104.	L02BG	Anastrozole	modest invention but opportune	1996	B
105.	L02BG	Letrozole	me-too Anastrozole	1997	C
106.	L02BG	Exemestan	me-too Anastrozole	2000	C
107.	L03AA	Filgrastim	•	1991	B
108.	L03AB	Interferon beta-1b	me-too interferon	1996	B/D
109.	L03AB	Interferon beta-1a	me-too interferon	1997	B/D
110.	L03AB	Peginterferon alfa-2b	interferon pegylated	2000	B
111.	L03AX	**Glatiramer**	true invention	2001	A
112.	L04AA	Tacrolimus	invention	1995	B
113.	L04AA	Mycophenolic acid	invention	1996	B
114.	L04AA	Leflunomide	invention	1999	B
115.	L04AA	**Etanercept**	true invention	2000	A

Number	ATC code	International name	Scientific inventiveness	Year of registration	Category
116.	L04AA	Sirolimus	me-too Tacrolimus	2001	B
117.	M01AB	Aceclofenac	me-too Diclofenac	1997	C
118.	M01AC	Meloxicam	me-too Piroxicam	1996	C
119.	M01AC	Lornoxicam	me-too Piroxicamu	1999	C
120.	M01AE	Dexketoprofen	isomer of Ketoprofen	1999	C
121.	M01AE	Dexibuprofen	isomer of Ibuprofen	2001	C
122.	M01AH	Rofecoxib	(withdrawn)	1999	C
123.	M01AH	Celecoxib	(still in use)	2000	C
124.	M03AX	Botulinum toxin	old toxin, new use	1993	B
125.	M05BA	Pamidronic acid	me-too Etidronic acid	1992	C
126.	M05BA	Alendronic acid	me-too Etidronic acid	1996	C
127.	M05BA	Risedronic acid	me-too Etidronic acid	2000	C
128.	M05BA	Zolendronic acid	me-too Etidronic acid	2001	C
129.	N02CC	**Sumaptriptan**	true invention	1993	A
130.	N02CC	Zolmitriptan	me-too Sumatriptan	1997	B
131.	N02CC	Naratriptan	me-too Sumatriptan	1997	B
132.	N02CC	Rizatriptan	me-too Sumatriptan	1998	C
133.	N02CC	Almotriptan	me-too Sumatriptan	2001	C
134.	N03AF	Oxcarbazepine	me-too Carbamazepine	2000	C
135.	N03AG	Vigabatrin	me-too Valproic acid	1992	C
136.	N03AX	Lamotrigine	•	1993	B
137.	N03AX	Gabapentin	•	1995	B
138.	N03AX	Topiramate	•	1998	C
139.	N03AX	Levetiracetam	isomer of Piracetam	2000	C
140.	N04BC	Pergolide	me-too Bromocriptine	1993	C
141.	N04BC	Dihydroergocryptine – mesilate	me-too Bromocriptine	1995	C
142.	N04BC	Ropinirole	•	1997	C
143.	N04BC	Pramipexole	•	1998	C
144.	N04BC G02CB	Cabergoline	me-too Bromocriptine	1995	C
145.	N04BX	Budipine	•	1997	C
146.	N04BX	Entacapone	me-too Tolcapone (withdrawn)	1998	C
147.	N05AE	Ziprasidone	me-too Sertindol	2002	C/D
148.	N05AH	Olanzapine	me-too Clozapine	1996	B
149.	N05AH	Quetiapina	me-too Clozapine	2000	C
150.	N05AL	Amisulpride	me-too Sulpiride	1999	C
151.	N05AX	**Risperidone**	true invention	1994	A
152.	N05CF	Zolpidem	me-too benzodiazepine	1991	B
153.	N05CF	Zopiclon	me-too benzodiazepine	1991	C
154.	N05CF	Zaleplon	me-too benzodiazepine	1999	C
155.	N06AB	Paroxetine	•	1992	C
156.	N06AB	Citalopram	•	1996	B
157.	N06AB	Sertraline	•	1997	C
158.	N06AG	Moclobemide	•	1991	C
159.	N06AX	Mirtazapine	me-too Mianserine	1996	B
160.	N06AX	Venlafaxine	modest invention but opportune	1996	B
161.	N06AX	Nefazodone	me-too Trazodone	1997	C
162.	N06AX	Reboxetine	•	1998	C
163.	N06DA	Donepezil	•	1997	B/D
164.	N06DA	Rivastigmine	me-too Pyridostigmine	1998	C/D
165.	N06DA	Galantamine	natural alkaloid	2001	C
166.	N07BB	Acamprosate	me-too GABA (learnt in 1952)	1996	C
167.	N07XX	Riluzole	•	1996	D
168.	R01AC	Azelastine	•	1992	C
169.	R01AC	Levocabastine	•	1994	C
170.	R01AD R03BA	Fluticasone	me-too Budesonide	1994	B
171.	R01CC	Bambuterol	me-too Salbutamol	1992	C
172.	R03AC	Salmeterol	me-too Salbutamol	1995	B
173.	R03AC	Formoterol	me-too Salbutamol	1997	B
174.	R03BA	Mometasone	me-too Budesonide	1993	C
175.	R03BB	Tiotropium	me-too Ipratropium	2002	B
176.	R03DC	**Montelukast**	true invention	1998	A
177.	R06AE	Levocetirizine	isomer of Cetirizine	2001	C
178.	R06AX	Fexofenadine	metabolite of Terfenadine	1997	B
179.	R06AX	Mizolastine	•	1998	C
180.	R06AX	Desloratadine	me-too Loratadine	2001	C
181.	R06AX	Ebastine	•	2002	C
182.	S01BC	Ketorolac	me-too Indometacine	1992	C
183.	S01EA	Brimonidine	•	1998	C
184.	S01EC	**Dorzolamide**	invention not original but opportune	1995	B
185.	S01EC	Brinzolamide	me-too Dorzolamide	2000	C
186.	S01EE	Latanoprost	me-too Dinoprost	1997	A
187.	S01EE	Travoprost	me-too Dinoprost	2002	C
188.	S01EE	Bimatoprost	me-too Dinoprost	2002	C
189.	S01GX	Lodoxamide	•	1997	C
190.	S01GX	Emedastine	•	1999	C

Legend. Categories A, B, C, D were taken from Germany where they mean:

A. Innovative structure generating a new way of drug's activity, and new therapeutic advantages.

B. Improved pharmacodynamic or pharmacokinetic properties of an old structure and method of acting.

C. Analog of the former medicine - not improving its method of acting or improving it insignificantly.

D. The method of acting insufficiently elucidated or a vague opinion about the drug's value.

Annex 2

Best selling drugs in the world 2005

Number	Medicine	Brand name	Producer's ingeniousness	Sales ($ in millions)
1	Atorvastatin	Lipitor, Sortis	me-too Lovastatin	12.986
2	Clopidogrel	Plavix	me-too Ticlopidine	6.345
3	Fluticasone + Salmeterol	Advair, Seretide	me-too Budesonide + Salbutamol	5.465
4	Amlodipine	Norvasc	me-too Nifedipine	4.706
5	Esomeprazole	Nexium	me-too Omeprazole	4.633
6	Simvastatin	Zocor	me-too Lovastatin	4.382
7	Olanzapine	Zyprexa	me-too Clozapine	4.202
8	Lansoprazole	Prevacid, Takepron	me-too Omeprazole	3.996
9	Valsartan	Diovan	me-too Losartan	3.676
10	Etanercept	Enbrel	true invention	3.657
11	Risperidone	Risperdol	true invention	3.552
12	Infliximab	Remicade	true invention	3.547
13	Venlafaxine	Effexor	modest invention but opportune	3.459
14	Pantoprazole	Protonix, Pantozol	me-too Omeprazole	3.428
15	Rituximab	MabThera	true invention	3.334
16	Epoetin alfa	Eprex	analog of Erythropoetin	3.324
17	Darbepoetin alfa	Aranesp	analog of Erythropoetin	3.273
18	Sertraline	Zoloft	modest invention but opportune	3.256
19	Alendronic acid	Fosamax	me-too Etidronic acid	3.191
20	Losartan	Cozaar	true invention but little advancement	3.037
				87.449

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The torch of the pharmaco-economic enlightenment

By nature, economists, lawyers, journalists and consequently, politicians are no experts when it comes to the knowledge of medicines. Thus their poor comprehension of the economics of drugs has made it possible for pharmaceutical companies to cheat on an unimaginable scale for years.

Already in the 1960s staggering price irregularities were publicly revealed in different countries, including the United States (Senators Kefauver, Harris, Humphrey), and the United Kingdom (Lord Sainsburry). It happened wherever people wanted to find out and address this problem. These irregularities were harshly criticized and resulted in a counteraction. In the USA, a ban on using the brand names of the registered medicines was considered (the registered names make it easier to trick both doctors and patients). In the UK, the Labour Party was even considering nationalization of the pharmaceutical industry.

However, subsequent wrongdoings involving pharmaceutical corporations died a natural death. Big pharma employed economists and medical doctors so they might prove not only how much good the pharmaceuticals do for the humanity (producing new and better medicines, lessening of human suffering and prolonging life) but also how many billions of dollars the companies spend to achieve these aims. The word has learned that drug manufacturers are benefactors and not plunderers.

Most probably governments and parliaments in countries hosting big pharmaceutical industry have realized that it is not in their interest to have a proper and fair price system (the costs plus a decent profit). It was worth it to permit manufacturers to fix high prices at home because this made it possible to sell medicines at high prices all over the world and bring home billions of dollars.

Two hundred countries deprived of the pharmaceutical industry have no way out. They have to pay if they want to have drugs. These countries need to be educated so they will pay high prices but only for the truly innovative medicines bringing pharmaceutical progress and they will not pay high prices for the pseudo-innovations, which do not offer a better treatment.

This "educational" work is a necessary response to the growing aggression of the big pharma. Consider the following example.

Economic liberalism in the USA that was uncritically transplanted into the pharmaceutical industry, lack of knowledge of medicines not only on the part of the federal but also state governments, as well as powerful lob-

bying of big pharma – have all resulted in prices of drugs being oppressively high. This problem has affected millions of people because the state has been helping to finance only those medicines that have been distributed to the veterans of the Vietnam War, the poor and since 2005 – also to the elderly.

Arnold Schwarzeneger, a politically influential governor of California, has recently appealed for cheaper medicines. He has not been alone in this. The Governor of Florida (President Bush's brother) has also been asking for reasonable prices of pharmaceutical products for quite some time.

Both are right. Drug prices in the USA are pathologically high. They are much higher than in Canada, Great Britain, Germany and so on.

Why? Outside the USA, there is more or less just view that the big pharmaceutical industry is monopolistic. A medicine is made by one maker (due to a patent or/and a brand registered name). Consequently, there is a price control outside the USA. Meanwhile, in the USA the big pharmaceutical industry persuaded the government and the parliament that the price control is unnecessary because the drug makers compete, which is not true. Their products compete with other monopolistic products. A competition of monopolistic products does not result in the price reduction. It results in the price escalation.

What has the big pharmaceutical industry done in response to Schwarzeneger/Bush's requests? Has it tried to contain its greed? No! Instead, it has lied that the Americans and only Americans have been bearing the enormous costs of pharmaceutical research and have been the victims of parsimony on the part of other countries, especially the European ones. That is why the Americans must pay high prices for medicines.

The lecture given by Ian Read, president of Pfizer Europe, published by a prestigious magazine think: act (Number 1/2006) and reprinted eagerly in other countries thanks to the efforts of pharmaceutical firms, might be given as an example of stupefying the public. In Poland, the article appeared in The Gazeta Prawna magazine, in the issue from September 15th.

Mr. Read proposed that:

1) Governments of European countries should finance the basic medicine research as it is done in the USA. Data needed by the industry is obtained in this way.

2) Governments of European countries should reimburse new monopolistic, very expensive medicines from public funds to ensure easy access of people to them (what a cheek! Mr. Read, president of a US company, does not demand this from the US Government, which does not reimburse anything for the majority of its citizens).

Mr. Read says that what Schwarzeneger has in mind is that American consumers have to pay high prices in order to finance drug research while European consumers don't pay. In the European Union, the governments tend to define (to limit) the term "innovations" (which are reimbursed) and

to contain the total drug expenditure in spite of the fact that the cost of prescription drugs constitutes only 15% of the health care costs.

Bent on the expansion of the expensive and monopolistic innovations, Mr. Read proposes giving a bigger degree of say-so to patients in choosing medicines for themselves. Doctors should not make decisions solely based on their own opinions. This proposal is evidently in favour of money makers. Let "the numskulls" have the biggest influence over the choice of drugs. This will facilitate sales of drugs that do not bring any pharmaco-economic progress.

Below is the pharmaceutical and economic response to the mind-boggling appeals of Mr. Read, president of Pfizer. We base our material evidence only on the drugs manufactured by Mr. Read's company. We do this not because we are lazy but because no one would like to read the truth about all pharmaceutical companies operating in the same manner. For similar reasons, we will limit our evidence only to the biggest Pfizer drugs (in terms of the value of sales). Everyone has the right to believe that the biggest turnover is generated by the most important inventions.

We examine all those Pfizer medicines whose turnover value exceeds $1 billion annually. None of them is a Pfizer's invention that would deserve the reward in the form of a high monopolistic price.

Atorvastatin (Lipitor, Sortis) with the turnover value of $12,187 million

Atorvastatin was not invented by Pfizer but by Warner Lambert (Parke Davis) – a company "swallowed" by Pfizer. But let us learn more essential facts:

1) Atorvastatin is not a true invention that required big financial investments in its scientific and research work. This was not an innovative idea but a scheme to line one's pockets with a "me-too" drug and exploit somebody else's invention (lovastatin and simvastatin).

If the patent law was not unreasonable but logical and fair, atorvastatin should have a 17-year-long patent protection starting from 1980 (invention of lovastatin) and not from 1991. As a drug no longer protected by a patent, it should be available throughout the world for $0.44/DDD (10 mg) starting from 1997.

Meanwhile Lipitor/ Sortis sells still in 2006 for:

In the USA (its biggest market)
A wholesale price of $ 291.25/100 tablets of 10-mg = ca $ 3.64/DDD

In Germany
A retail price of Euro 102.61/100 tablets of 10-mg = ca $ 1.36/DDD

In Poland
A retail price of ZL 80.61/30 tablets of 10-mg = ca $ 0.90/DDD

One might assume with a some degree of error that Pfizer charges throughout the world an average price of ca $ 2.32/DDD when the correct and justified Pfizer's price should come (because it might be easily obtained at such a price) at maximum of $0.44/DDD

Thus the price is five times higher than it should be. For a pseudo-invention that did not require expensive research, Pfizer undeservedly fleeces its customers out of $10 billion annually !!! [12.187 x (2.32 - 0.44)]: 2.32 = 9.876.

2) It sometimes happens that a medicine made by "a sheer fluke" and not due to spending a lot of money on research and development is better. It happens rarely but it does happen. For example, hydrochlorothiazid was considered to be a better medicine than chlorothiazid. This fact speaks in favour of letting the industry produce congeners, the "me-too" drugs, the pseudo-inventions although in the majority of cases, they are inferior. The inferior congeners do not cause much harm because doctors prescribe them rarely.

Atorvastatin has not caused too much harm either. According to the experts with authority, e.g. NICE (National Institute for Clinical Excellence), it is as effective as other statins. However, if it is not better, there is no justification to pay Pfizer $10 billion more for it on the yearly basis.

Instead of being shamed and giving us back these $10 billion obtained unjustifiably, Pfizer is cheeky enough to lecture European governments not to bargain and to promote higher consumption of atorvastatin by reimbursing it – as an invention that has raised health care to a higher level.

Amlodipine (Norvasc) with the turnover value of $ 4,706 million

Amlodipine is not an original idea either and its realization has not required investing many millions of dollars into research and development. It is one of many derivatives of dihydropyrimidine, made in 1983 from the same mould as Bayer's nifedipine in 1968. In moral terms, it did deserve the patent protection until 1985. Legally, it lost the patent protection only in 2000.

Pfizer has committed a moral offence by charging for the drug in 2006 a wholesale price of $171.82 for 100 5-mg tablets. The Polish pharmaceutical company can provide identical amlodipine for the wholesale price of $32.60/100 5-mg tablets. A hundred of other companies might do the same. So an obvious conclusion comes to mind – by taking advantage of consumers' lack of knowledge of medicines, Pfizer robs them out of $3.8 billion annually !!! [4,706 x (17.18 - 3.27)]: 17.18 = 3.810. It is a shame!

If that was not enough, Pfizer cynically demands that cautious European governments do not bargain and agree to pay a five-time inflated price and still reimburse it from public funds.

Sertraline (Zoloft) with the turnover value of $3,256 million

Sertraline is not a copy of the earlier inventions made by someone else like the selective serotonine reuptake inhibitors (fluoxetine, fluvoxamine, citalopram). The idea is original and it is an antidepressant. However, it is not a new drug – the patent is from 1981 so its inventor has had enough time to recover his expenses on research and development and make good profits. Once the patent protection expires, Pfizer should start competing with other companies. Competitive retail prices in Poland are in 2006):

Sertraline (Asentra, Krka)	tablets: 50 mg x 28	PLN 43.84
Sertraline (Luxeta, Pliva)	tablets: 50 mg x 28	PLN 25.47
Sertraline (Sertahexal, Hexal)	tablets 50 mg x 28	PLN 22.18
Sertraline (Setaloft, Actavis)	tablets 50 mg x 28	PLN 27.72
Sertraline (Setaratio, Ratiopharm)	tablets 50 mg x 28	PLN 26.57
Sertraline (Stimuloton, Egis)	tablets 50 mg x 28	PLN 41.24
Sertraline (Zotral, Polpharma)	tablets 50 mg x 28	PLN 38.41
	An average generic price	PLN 32.21

Mr Read's price in Poland is:

Sertraline (Zoloft, Pfizer)	tablets 50 mg x 28	PLN 72.96

In Poland, Pfizer has been very restrained – it has only charged 126% too much in comparison with the average generic price.

In the USA, such an amount of Zoloft has a wholesale price of $81.07 = PLN 243.21 – 655% too much.

In Germany, such an amount of Zoloft has a retail price of EUR 51.04 = PLN 204.29 – 534% too much.

There is no compassion for people who suffer from depression.

Azithromycin (Zithromax) with the turnover value of $2,025 million

Pfizer did not even spend one cent to develop azithromycin. As its inventor – Pliva did not have a distribution network in the USA, it signed a license agreement with Pfizer. In the agreement, Pliva did not include the accuracy clause of prices. Pliva did not think that Pfizer still might be able to charge in 2006 a monopolistic price for an old invention, especially in view of the fact that the invention was not that original in the first place. Azithromycin was a clone of roxithromycin made by French Roussel and clarithromycin manufactured by Japanese Taisho, antibiotics invented earlier – in 1981. The idea involved a small synthetic alteration of an old macrolide antibiotic – erythromycin, sold cheaply by Polfa Tarchomin in Poland among others.

The cheapest generic azithromycin we know costs PLN 35.98/6 x 250 mg.

Pliva, inventor of azithromycin, charges for the Sumamed brand PLN 66.35/6 x 250 mg.

Pfizer, license holder, charges for the Zithromax brand in the USA a wholesale price of $52.76/6 x 250 mg = PLN 158.27/6 x 250 mg - 4.4 times too much.

Therefore, in the case of azithromycin, Pfizer is not entitled in any legal, commercial or moral terms to urge governments of European countries to buy and reimburse its Zithromax. Pfizer should rather confess to governor Schwarzeneger that it has been cheating American consumers out of its pure and unrelenting greed.

Celecoxib (Celebrex) with the turnover value of $ 1,730 million

2006 prices are as fallows:

– pharmacy purchasing price in the USA – USD 2,04/100 mg
– pharmacy selling price in Poland – EUR 1,00/100 mg
– pharmacy selling price in Germany – EUR 0,68/100 mg
– pharmacy selling prices in France – EUR 0,50/100 mg
– pharmacy selling prices in Great Britain – GBP 0.36/100 mg

It means that retail prices in the USA are 2.8 times higher than in Poland and 3.8 times higher than in France and Great Britain.

Irrespective of the exaggerated prices, the value of Celebrex sales has been falling drastically – it was $3,302 million in 2004; while in 2005, only $1,730 million. Certainly it is a consequence of a very bad experience with its sister-drug Vioxx (rofecoxib), which was withdrawn from the market. Both chemical and pharmaceutical similarities between celecoxib (Celebrex) and rofecoxib (Vioxx) inspire justified fears in doctors who do not want to use celecoxib, although it is not banned, as not to harm their patients.

Let us also mention that celecoxib (Celebrex) was invented by Searle and not Pfizer.

Sildenafil (Viagra) with the turnover value of $1,645 million

It is an especially profitable drug. In fact, it does not really provide a medical treatment of erectile dysfunction but only temporarily improves male sexual potency. By its nature, it creates a quite big interest so one cannot really explain why the sales of the drug have not been increasing: in 2004 – $1,678 million, in 2005 – $1,645 million.

But in any case, Pfizer has still been incredibly lucky. It did not invest much money into this invention. Sildenafil was a godsend to Pfizer. During clinical trials of a potentially cardiologic medicine in which some healthy young men volunteered to participate, sildenafil's "miraculous" and not cardiologic properties were "discovered." It was a rare coincidence, which resembled an old case of Largactil (chlorpromazine) made by Specia in Paris many years before. Scientists were searching for better Phenergan (promethazine) – a better anti-histamine drug and accidentally a schizophrenic patient was cured. A breakthrough in neurology/ psychiatry was achieved without any costly research.

However, we do not deny the right of Pfizer to make profits from Viagra. It should make as much money as it wants. We do deny its right to approach European governments and demand that they reimburse the drug and by doing so increase Viagra's turnover and Pfizer's profits in recompense for an imaginary high cost of R&D.

Latanoprost (Xalatan) with the turnover value of $1,372 million

As a complement to very good but not ideal medicines to treat glaucoma such as pilocarpine and timolol, prostaglandines do constitute some progress. However, is Pfizer entitled to demand more than it already has? No, it is not.

Firstly, Pfizer did not invent latanoprost. Two companies, not only Kabi but also Chinoin, pretended to obtain a patent for the drug.

Secondly, the invention of latanoprost in 1993 was not original enough to shower its inventor with gold. Unoprostone, made in 1988 in Japan and patented by the Ueno Company, was an original invention. Latanoprost is a simple "me-too" drug. We wish it well but only if it is sold at reasonable price – but it is not. Xalatan (latanoprost) costs in Poland PLN 64,60/2,5 ml White Philocarpine is available at PLN 4,40/5 ml and Timolol at PLN 5,04/5 ml.

Cetirizine (Zyrtec) with the turnover value of $1,362 million

Pfizer had nothing to do with the research work involving an invention of cetirizine. It was a quite auspicious invention made by a modest Belgian company – UCB (Union Chimique Belge) and patented in 1982. Pfizer has always been eager to profit from someone else's inventions so it bought the license from the Belgians.

The idea of cetirizine was not original even on the day it was realized. It was a small chemical alteration of the benzhydrylpiperazine structure. As early as 1953, we had cyclizine and chlorcyclizine from Burroughs Wellcome and in 1955, buclizine and meclizine from UCB. Cetirizine proved to be a bit better but its inventor did not deserve to be showered with gold. UCB knows this and sells its Zyrtec at quite reasonable prices – PLN 0.71/DDD (10 mg). In generic sources, cetirizine might be purchased for as little as PLN 0.45-0.63.

Meanwhile Pfizer desires the US pharmaceutical industry expansion into Europe with the US wholesale price of its Zyrtec on a UCB license at $69.83 for 30 10-mg tablets. After calculating the exchange rate, it turns out that the Pfizer price is twelve times higher than that of original European Zyrtec and nineteen times higher than that of a cheap generic product!!!

After reviewing the biggest moneymaking Pfizer's medicines sold for $28 billion at producer's prices, which constitutes 50% of company's business, let us go back to Mr. Read's lecture. One might get an impression

that President Read has absolutely no idea of what he is talking about. As if he did not know about his customers being robbed both in and outside of the USA. As though he believed that he would be able to stop robbing American consumers by convincing governments of European countries to pay for his drugs more than they have been doing so far. As if he was deeply convinced that his company deserves to be compensated by Europe and the world for its gigantic investments into research and development, while in reality, it has born almost no expenses (except spending money on promotion and lobbying).

We will send a copy of this article to Mr. Read. Let him take up the gauntlet and reveal his calculations of prices and costs – let him reveal his company's true expenditures on innovations.

* * *

Tadeusz J. Szuba

Look at EU drug policy

The European Commission established the Pharmaceutical Forum in June 2005 to examine the competitiveness of the European-based pharmaceutical industry. In fact, the advantage is on the US side. The United States develops more new drugs while Europe - not as many. Sales of American pharmaceutical companies grow faster.

The Commissioners don't know the reasons of American superiority. They confide in the big pharma's propaganda that a process of innovation is terribly costly, that American companies are able to invest because nobody disturb them to make profit. There is not price control in the USA, there is not limiting the reimbursement. Recently there is unrestricted law of promoting to the public not only OTC drugs but Rx drugs too.

The Commissioners don't know that the number of innovations says very little, there are very few real innovations, there is plenty of pseudoinnovations, of "me-too drugs".

The Commissioners don't know that producers of me-too drugs are making profit with the help of marketing force (in general the budget for marketing is several times higher that the budget for research & development) and the help of law allowing them to have patents for "me-too innovations". Gradually, drugs are like other goods, more cookies for personal satisfaction than the weapon in physician's hand to fight the disease. Interestingly, according to big pharma, the patients, not physicians, are the judges of the quality of medicines.

High prices and profits in the USA did not influence the innovativeness; the number of new American drugs is dramatically falling. Despite this fact the European Commission looks for facilitating profits in the European drug industry. It intends to recognize all new drugs as innovative ones and deserving reimbursement.

Logically, the Pharmaceutical Forum, called into being by the Vice-President Verheugen, had to take forward the following crucial issues, in particular:

– Information to Patients,
– Relative Effectiveness,
– Reimbursement.

Information to Patients.

There are millions of drugs all over the world. Many of them are not excellent. Some of them bring more injury than good. Ordinary people are unfamiliar with the science of pharmaceutical commodities. In order to protect the people, the governments set up the law:

– Drugs potentially harmful are dispensed on doctor's prescriptions only,

– Information (promotion) of prescribed drugs is addressed to professionals only (doctors and pharmacists).

Recently, the big pharma extorted from the American Parliament the permission to advertise Rx drugs to the public (in the press, radio, television). Perhaps the damages are not disastrous because US citizens are prudent and have access to doctors. Before using an advertised drug, they ask a medical professional for advice.

There is actually a big pharma's pressure in Europe on the free promotion of prescription drugs. The European Commission would like but has no courage to do so, therefore, it has started to prepare the Pharmaceutical Forum to the turn for the worst. Astonishingly, the Forum consisting of doctors did not condemn the big pharma's stand that doctors looking for quality of drugs obstruct the human well-being.

Our doctors evidently know best that in Europe the industry's dream of patients deciding what to cure with what is surrealistic.

The question addressed to the Pharmaceutical Forum concerning the free information to patients on Rx drugs will be certainly answered negatively.

Relative Effectiveness and Reimbursement.

Therefore, the main subject of Forum's interest is the relative effectiveness and reimbursement. These points are very close to each other. In Europe, there is no reimbursement of ineffective drugs. In Europe, the assessment of effectiveness is very important.

The matter is very complex when most new drugs ("me-too drugs") are

made for money and not to give health. Their effectiveness is not better but sometimes slightly different. Inventors (companies) stress positive elements and make no mention of imperfections.

The government or the governmental insurer has to decide what to reimburse. The decision would be easy if only the criterion of quality was taken into consideration. Following "me-too" drugs are very similar, many are worse than their predecessors but the difference (in disfavor) is not great, once the drug agency allowed them to be sold.

The governmental problem has an economic nature because "me-too drugs" may differ much in price. An original drug after the period of patent protection becomes cheap due to competition. A me-too drug is always invented later. Its patent protection starts later and its monopolistic high price lasts longer. The use of a "me-too drug" not better and very often worse – it may cost the government (or patients) millions EURO.

It happens quite often that "me-too drugs" of inferior quality, rarely prescribed by doctors, do not inspire competition. They are always expensive – also after the patent validity expiration.

Governments should demand a modification of TRIPS for pharmaceutical products from the World Trade Organization. All "me-too drugs" are not real inventions. They are easy remakes of the previous and real inventions. They should be protected by patents only as long as the real inventions are.

Look at the explanation of our proposal:

Table 1

Me-too ACE inhibitors				
Nº	Medicine	Year of invention	20 year protection till	
			Actually	Should be
1	Captopril	1977	1997	1997
2	Enalapril	1980	2000	1997
3	Lisinopril	1980	2000	1997
4	Delapril	1982	2002	1997
5	Fosinopril	1982	2002	1997
6	Moexipril	1982	2002	1997
7	Perindopril	1982	2002	1997
8	Quinapril	1982	2002	1997
9	Benazepril	1983	2003	1997
10	Cilazapril	1983	2003	1997
11	Imidapril	1983	2003	1997
12	Ramipril	1983	2003	1997
13	Trandolapril	1983	2003	1997
14	Spirapril	1984	2004	1997
15	Temocapril	1985	2005	1997

Table 2

Me-too HMG CoA reductase inhibitors				
Nº	Medicine	Year of invention	20 year protection till	
			Actually	Should be
1	Lovastatin	1980	2000	2000
2	Simvastatin	1981	2001	2000
3	Pravastatin	1981	2001	2000
4	Fluvastatin	1984	2004	2000
5	Cerivastatin	1989	withdrawn	
6	Atorvastatin	1991	2011	2000
7	Rosuvastatin	1998	2018	2000

There is a very long procedure of changing the patent law for drugs by the WTO, which is dominated by the USA. The "me-too drugs" invented later will remain protected by patents for a long time after the expiration of the patent protecting a real invention.

European governments impede a little bit the reimbursement of the "me-too drugs" that are more expensive but not more effective. They are certainly right. They are responsible for health, for the accessibility of drugs while their health budgets are limited.

An excellent instance of the national drug policy is the NICE pronouncement in England that me-too statins are equally effective and the National Health Service should reimburse the cheapest ones only.

EU drug policy.

The European Commission seems to be double-faced, even Pharisaical. One says:

The Pharmaceuticals Forum has created the Working Group on Relative Effectiveness with the mission to support the Member States in applying the Relative Effectiveness systems in order ***to allow containment of pharmaceutical costs*** *as well as a fair reward for innovation. The outcome of relative effectiveness is promising as it will help identify the most valuable medicines, both in terms of clinical efficiency and cost-effectiveness, as well as it will help set a fair price for these medicines.*

Then we notice any step toward containment of pharmaceutical costs and many steps toward the American way of drug policy. The most important is the obliteration of difference between a real innovation and a pseudoinnovation ("me-too drug"). Evidently. Europe and the whole world is interested in real innovations.

The activity of Relative Effectiveness Group created by the Commission, is going opposite direction. After 12 months of intensive work the Group did not agree on the definition of innovation ! The Group evidently accepted the point of view of big pharma: everything is the innovation, "innovation is the continuum". However, without definition how the fair reward for innovation could be appointed? Such reward for industry to develop real breakthrough innovation is also a big reward for all sick people and

such should be the understanding of the mission stated by the Commission to the Relative Effectiveness Group.

We suggest that our European health ministers instruct their delegates-members of the Working Group within the Pharmaceutical Forum not to follow the American way of doing the pharma business. It is the worst way in the whole world.

See the data below:

Table 3

Medicine dosage, producer	AWP price in USA USD	Retail price in France EUR	Price relation France:USA
1	2	3	4
Atorvastatin tab. 10 mg, Pfizer	Lipitor 2.77	Tahor 0.91	1.00 : 2.77
Clopidogrel tab. 75 mg, BMS	Plavix 4.67	Plavix 2.13	1.00 : 1.99
Fluticason + Salmeterol dose 100/50 mcg, GSK	Advair Diskus 2.44	Seretide Diskus 0.71	1.00 : 3.13
Amlodipine tab. 10 mg, Pfizer	Norvasc 2.36	Amlor 0.62	1.00 : 3.46
Esomeprazol tab. 20 mg, Astra Zeneca	Nexium 5.06	Inexium 1.20	1.00 : 3.83
Simvastatin tab. 20 mg, Merck&Co	Zocor 5.25	Zocor 0.98	1.00 : 4.87
Olanzapine tab. 10 mg, Eli Lilly	Zyprexa 11.76	Zyprexa 4.18	1.00 : 2.56
Lansoprazol tab. 30 mg, Takeda	Prevacid 4.93	Lanzor 1.66	1.00 : 2.70

Remarks:

1) In the USA there are not retail prices; pharmacy owner is free in fixing the price. We have taken the Average Wholesale Prices from the Red Book 2006 and added 20%.

2) In continental Europe there are fix retail prices. We have taken them from France from the Dictionnaire Vidal 2006.

3) In order to calculate the relation of prices applied in the USA and France we have used the currency exchange rate recorded in London on the December 22nd, 2006: EUR 1.0000 = USD 1.3195.

Drug prices in the USA are 2-3-5 times higher than in Europe. American profits are enormous. They are wasted, are spent on the promotion of unnecessary "me-too drugs". America and the whole world receive almost nothing in return.

We suggest that our health ministers instruct Working Group members to say "no" with regard to the EU crucial issues:

– no to the information to patients on Rx drugs,

– no to the relative effectiveness; the effectiveness must be real and well documented,

– no to the reimbursement of big pharma's pseudoinnovations; reimbursed should be medicines most effective and least costly.