medical ethics
patient orientated pharmacology

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General assembly of Bayer stockholders Cologne 27th.May.2015
Compliant letter of Mrs. Valerie William.

Mr. Wenning, Dr. Dekkert,
Please find the letter of Mrs Valerie Williams regarding your behaviour at the assembly, which I do consent upon entirely.

Furthermore, I relate to the article published by Spiegel number 43/ in 1977, delivering clear evidence on what Primodos did to so many victims in Britain. A more detailed view on the various adverse effects of the drug can be seen and further detailed in the Uppsala Monitoring Centre, as shown below.

- Blood and lymphatic system disorders (33)
- Cardiac disorders (153)
- Congenital, familial and genetic disorders (75)
- Ear and labyrinth disorders (17)
- Endocrine disorders (12)
- Eye disorders (114)
- Gastrointestinal disorders (262)
- General disorders and administration site conditions (476)
- Hepatobiliary disorders (172)
- Immune system disorders (12)
- Infections and infestations (79)
- Injury, poisoning and procedural complications (73)
- Investigations (200)
- Metabolism and nutrition disorders (50)
- Musculoskeletal and connective tissue disorders (152)
- Neoplasms benign, malignant and unspecified (incl cysts and polyps) (757)
- Nervous system disorders (654)
- Pregnancy, puerperium and perinatal conditions (320)
- Psychiatric disorders (299)
- Renal and urinary disorders (17)
- Reproductive system and breast disorders (437)
- Respiratory, thoracic and mediastinal disorders (408)
- Skin and subcutaneous tissue disorders (381)

- Social circumstances (20)
- Surgical and medical procedures (17)
- Vascular disorders (943)

Why therefore putting the most vulnerable at risk, if there is no need to do so?! Medicine clearly is about administering the necessary rather than the wanted or servicing the *"convenience of physicians in diagnosis"*. It is all about protecting patients rather than submitting them to try and error.

Mr. Dekkert you repeatedly claimed during the assembly, that Bayer is convinced that drugs that were criticised are useful, necessary and benefit the patients treated with them. Well what does that mean in the sight of these facts? It is nothing but the trivial chit- chat of somebody defending the interest of a company, in a situation where there is nothing to defend, but much to admit. In essence, it is violating the human rights of the week and neglecting the needs of those that were scattered for the rest of their life, while they yet did not enter into their physical existence.

Mr. Wenning, most of us are mothers and fathers and it is our sacred obligation to protect our children from any harm, that may threaten them and to foster them in times of need. If a mother so does, all the power that the chairman of the advisory board has, is to switch of the microphone and stop the utterance of a devastated, suffering herself from more than 20 operations, facing the next one and in constant awareness of her son, who was severely physically disabled, by the drug that was inflicted on him, while still in his mothers womb.

What a remarkable achievement that is, Mr. Wenning. My father an enterpriser always taught his sons, that men have an obligation to protect women from harm, rather then to inflict it on them and right he was!

Mr. Dekkert you noted in your speech, that you were much concerned about the attitude of the "stakeholders" of society turning against the pharmaceutical industry. Are you not able to see, that it is the behaviour of pharma managers, which leads to this attitude? What should a stakeholder or a citizen think about this industry, when she/he hears the following?

Quote from Mrs. Kathleen Sebelius Health & Human Service Secretary of the United States of America, regarding the settlement against Pfizer about the illegal promotion of drugs:

> *"…..they didn't just implicate Pfizer; they actually identified in charge the senior managers, who were responsible for the fraud."*

(Source: https://www.youtube.com/watch?feature=player_embedded&v=SsBaCSNd_6c)

James Cole Deputy Attorney General of the United States of America, regarding the settlement against Glaxo SmithCline, gave a similar address to be seen here:
https://www.youtube.com/watch?feature=player_embedded&v=IuoZWLUsj38

Misbehaviour of pharma managers constantly gets to the attendance of political stakeholders and legal officers. These are just two cases of a list that is much longer.

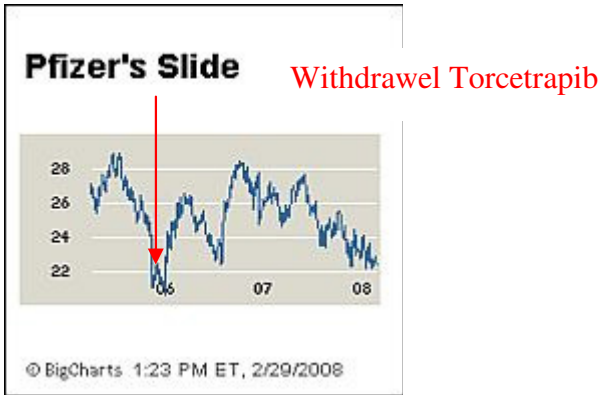
Analyzing these situations more fully reveals the cause. Talking in the terms used in pharma marketing, one mayor issue, always present in the respective literature, is "accelerating the uptake of a product". Now even native English speakers often time find it hard to understand,

what is behind that terminology. It means, that the introduction of a product must be as speedy as possible, to insure success of this product in the market in the years to come. It is advertised massively, even though knowledge about its risks is very limited.

Launching new products, everybody finds it important to be successful. In fact, shareholders measure the worth of a pharmaceutical company in relation to its ability to successfully bring products to the market. This is so because members of the board of directors of these companies travel around the world visiting investors conferences, in order to present their lists of products that are currently under research. They do this in order to motivate investors to purchase their stocks. Institutional investors are of course much preferred, due to their tendency to purchase large amounts of stocks. They do so, calculating future revenue and margin possibilities of the company; they want to purchase stocks from.

The investment taken therefore is primarily based on estimating on future developments of a company. In consequence, failures become fatal, right?! This involves products on the trial list, prior to their introduction to the market and all those products that were approved and did not succeed in sales, after being brought to the market.

Want an example? Well here it is



Still remember? The drug had to be withdrawn from the trial list, in a very late state of developement. (It took 31 deaths in the clinical trial to find that out) Pfizer's shares suffered a loss of 10% in on the very day, facing massive consequences in many ways. Mayor consequence: Investors sued Pfizer for their losses. Pfizer announced to release 10.000 of their employees, on the very day. Did they have time to even consider consequences?

This is what you and your peers fear, it is the only fear. Adverse effects of the victims become secondary, if not even worse.

Is there an underlining problem? Sure there is. Do you address it? No, you do not! With time to the market literally cut in half, after the Contergan crisis, there is not enough time for careful clinical research. After this is done and the product is beaten through the regulators procedure, pharma producers rush into the market, turning on the marketing after burner. The consequence is that far too many people are severely burned or killed in this procedure. Substantial investments in the future are not possible. Primodos is the past, now comes the future.

As seen with the new oral anticoagulants (NOAK), it now takes more than one company to turn a market upside down, a truly new dimension in pharma marketing. Looking at the Rocket – AF® study being performed against a Warfarin control group with a

TTR of only 58.8% where a TTR of 70 % is the standard, it is very hard to believe, that a product has been approved, based on week data like that. Here is the outcome?

	Warfarin ADRs 47 years	**Xarelto** ADRs 7 years	**Pradaxa** ADRs 7 years	**Eliquis** ADRs 4 years
registered cases of advers effects	**66927**	**25021**	**38700**	**4991**
Blood and lymphatic system disorders	6092	1925	3771	183
Cardiac disorders	3029	1343	3072	275
Congenital, familial and genetic disorders	198	34	82	3
Ear and labyrinth disorders	305	166	219	37
Endocrine disorders	147	49	55	4
Eye disorders	1234	712	850	139
Gastrointestinal disorders	15801	5960	16087	1106
General disorders and administration site conditions	14506	4259	6271	680
Hepatobiliary disorders	768	479	448	80
Immune system disorders	475	122	142	46
Infections and infestations	2417	769	1787	161
Injury, poisoning and procedural complications	6815	3139	4123	583
Investigations	26368	3543	4448	450
Metabolism and nutrition disorders	1679	434	950	77
Musculoskeletal and connective tissue disorders	2977	1466	2224	298
Neoplasms benign, malignant and unspecified	679	264	573	72
Nervous system disorders	11121	4971	8339	1116
Pregnancy, puerperium and perinatal conditions	149	14	3	4
Psychiatric disorders	1813	631	1112	126
Renal and urinary disorders	4452	1771	3261	246
Reproductive system and breast disorders	845	653	389	61
Respiratory, thoracic and mediastinal disorders	7936	3958	4599	470
Skin and subcutaneous tissue disorders	6669	1817	2417	549
Social circumstances	352	134	116	11
Surgical and medical procedures	657	800	683	97
Vascular disorders	9437	4866	5025	570
Advers effects per registered report	1,9	1,77	1,84	1,49
Total adverse effects	126921	44279	71046	7444
Advers effects accumulated in years	47	7	7	4
ADRs reported p.a. since approval of indiv.NOAK	2700	6325	10149	1861
Extrapolation to 47 years	126921	297275	477003	87467
Warafarin ADRs 2003 - 2015	3921			
Factor of increase/ decrease reg. Extrapolation	1	2,34	3,76	-0,39
Records per age group 45- 64 in %	18	13	8	8
Records per age group 65- 74 in %	22	19	16	18
Records per age group ≥ 75 in %	37	35	35	42

Of course, it is difficult to compare these data directly. Therefore, this calculation is designed to deliver an indication in order to estimate, where it may end up with. Prof. Glaeske announced to deliver further evidence.

Well let us look at the “uptake of ADRs”
ADRs reported per year

	Xarelto	Pradaxa	Eliquis
2015	5150	4354	2318
2014	11549	10002	2437
2013	4740	5491	190
2012	2376	10320	43
2011	695	8071	70
2010	627	371	
2009	244	197	
2008	51	26	

Source Uppsala Monitoring Centre, WHO Database on adverse effects, based on registered reports filed from about 100 countries.

If time to the market is the problem and it is, why don’t you work on the problem? Have there been any ideas to solve this problem? Well not that I heard of.

This is what I hold you and your peers accountable for. You are sitting there gaining massive salaries, taking everything for granted and do not even attempt for substantial changes. The consequence is that drugs enter the market that are premature. However, they are presented to physicians, as if there has never before been anything that exceeds this new drug in safety and efficacy. Marketing starts even before approval of the drug, by massively manipulating the scientific scene.

Followed by massive adverse effects and the unnecessary sufferings and death of so many. Drugs that are withdrawn from the market, however as seen with Viox or Avandia, they are withdrawn only very shortly before their patents expire. What a diabolic game that is!

Well Mr. Dekkert I do wonder, why you are contemplating about stakeholders. The evidence is clear and in an information society, it is available to everybody. What if the patients, who in the end have to take these new drugs, become stakeholders to the extent, that they totally lose their confidence in novel drugs and refuse to take them? Impossible? Today you are fighting the problem of not being able to recruit new participants for clinical trials in the developed countries, which was not really a problem decades ago. Patients refusing to take new drugs is just the next, natural step in this story. Is this the reason, why therapy guidelines and diagnostic scores are so massively influenced by the industry, so doctors do not have a chance but prescribing anything else but novel drugs?

Abraham Lincoln once said:

> *“You can fool all the people some of the time and some of the people all the time, but you cannot fool all the people all the time”.*

Could there be a solution? Sure, it could. Call it patent under research, which would be a preliminary patent, to do the research properly, take all measures possible to ensure patients safety and come to the market offering a mature drug. The patent to market the drug, would be granted after the approval by the regulators. The time of the drug under regular patent in the market, would be the time it has been before the Contergan crisis, about 20 years.

Would other branches of industry profit from a like procedure? Sure, they would, in a world where research becomes ever more important and time for research increases substantially.

However, you stick with the problems that you have, do not work on the underlining problems and if patients confront you with their problems that arise of your misconduct, you switch of the microphone. Else, you quote answers that were formulated by others, from yellow pages.

This party will be over at some time. Only question is, how many people will have suffered and died in the end. What will remain of your proceedings? Dividends.

I have seen this to come decades ago. This is why I left this industry in 2004. Today I feel ashamed of serving this aberration for so many years of my life.

Homo homini scara res et danai non timeo

Roland Holtz