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Newsletter

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ISDB 2018 Newsletter and Update of activities

Welcome to the first ISDB newsletter of 2018 in which we report some interesting developments across the ISDB-community. Recently, Christophe Kopp announced that the next General Assembly will be organised by La revue Prescrire in Paris. The dates are Thursday until Saturday 10-12 October 2019 and the meeting will be held in the Prescrire meeting rooms near the office of Prescrire. A major topic to be discussed is the way ISDB bulletins have arranged their policy on Conflict of Interest (Col) following agreement of the ISDB Col statement in Leiden in 2016. As a reminder of this major issue, the items to be implemented by full members are printed on page 3. The ISDB Committee met in Utrecht, the Netherlands, in May and there is a short summary of the meeting on page 2. We have a new member from Spain, NoGracias and the team members introduce themselves on page 6 and 7. Currently, there is one active Working Group, the Clinical Trials Group from the United States (led by Nuria Homedes) and they report their activities on page 4 and 5. There is an initiative by the Cochrane Collaboration to set up guidelines on how to include Clinical Study Reports in their reviews and an ISDB Working Group on this issue might be launched in the future. A short summary of the activities related to this is presented on page 5. The ISDB website has been updated and we ask all members to check whether the contact details for their organisations are correct.

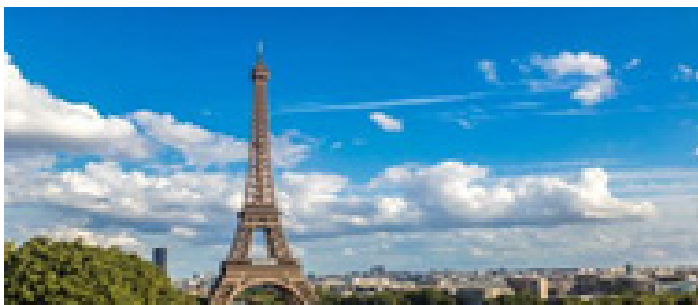
Finally, there are two reports from campaigns that ISDB has initiated in collaboration with the Dutch organisation Wemos (<https://www.wemos.nl/en/>), a global health foundation that also is involved in medicines. They organized a meeting in the European Parliament entitled 'How long is the arm of Big Pharma'. The other event was in Amsterdam where ISDB and Wemos organized a debate between Nicholas Freudenberg, distinguished professor of Public Health in New York, and some experts on the topics he discussed. His book Lethal but Legal describes the interrelationships between six big multinational companies that produce tobacco, food, alcohol beverages, medicines, weapons and cars. Nicholas Freudenberg also spoke in the European Parliament on the same topic. On page 12 you'll find the rapid response to BMJ after the expulsion of Peter Gøtzsche from the Cochrane Board.

Contents

News from ISDB (Extra) General Assemblies	2	Changes in membership-status	6
ISDB General Assembly Paris 2019		New members: NoGracias	
News from ISDB Committee Meeting Utrecht 2018			
Special attention to:	3	Actions and campaigns	8
Conflicts of interest		How long is the arm of Big Pharma?	
Updated website		Legal but Lethal	
Working groups	4	Cochrane's sinking ship and conflicts of interest	12
Clinical Trials Group			
Clinical Study Reports?			

ISDB General Assembly Paris 2019

La revue Prescrire is glad to host the next General Assembly in Paris (France). This will be a wonderful opportunity for Prescrire staff to meet colleagues from around the world, and for you to visit our office and the ISDB library, maintained by Minata Traoré at Prescrire since the creation of the society.



Save the date: Thursday to Saturday 10-12 October 2019.

Location: Prescrire's meeting rooms, not far from Prescrire's office

68-70 Boulevard Richard Lenoir.

The premises are located in the 11th district near Place de la Bastille, le Marais, Picasso museum.

More information about hotels and logistics will follow in due time.

Contact person:

Christophe Kopp

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ISDB Committee Meeting in Utrecht

The annual meeting of the ISDB Committee took place on May 5th and 6th in Utrecht, the Netherlands. Apart from organizational and financial matters, advocacy and working groups, a major discussion point was the way in which the conflicts of interest will be handled. This point is discussed on page 3.

Other important points were the updates of the membership status of full and associated members. The changes will be implemented in the website and again we ask members, full and associated, to check the data of their bulletins and organizations on the website.

Another important point were the quality checks of the bulletins. ISDB Committee performs this task every 3 years and all the full members will be assessed by the end of July this year. At the next General Assembly the Committee will give feedback on these checks.

Furthermore, we discussed how ISDB can be opened for other actors in the field of pharmacotherapy that support the realisation of rational pharmacotherapy. Meanwhile this has resulted in the acceptance of a Spanish organization NoGracias as an associated member of ISDB. They present themselves in this Newsletter on page 6 and 7.

The next meeting of the ISDB Committee will take place in February 2019.



ISDB Committee members:

Christophe Kopp, Rita Kessler (Prescrire's lobbyist for the European Parliament), Joerg Schaaber, Dick Bijl, Maria Font, Luis Carlos Saiz Fernández, Benoit Marchand and Ciprian Jauca.

Special attention to:

Conflict of Interest

The new ISDB-policy on conflicts of interest (Col) that has been approved in the Extraordinary General Meeting in Leiden 2016 and has been communicated already several times to you. The new policy applies immediately for new ISDB members. Existing members have been entitled to a three-year transition period, starting June 2016, to comply with the provisions of the rules. So, in the General Assembly in Paris 2019 bulletins are invited to show how they have executed this policy. We hope you are all able to be present there, but those who cannot attend the meeting are asked to show in writing and referring to their websites how they implemented the policy. Here is a small recap of the main changes related to the definition of Col: the independence of the editorial team and the organizational structure.

Definition: Conflict of interest with the healthcare industry

Any financial or advisory relationship (paid or unpaid) with the pharmaceutical industry or related healthcare

products industry (e.g. medical devices or diagnostics), including the conduct of industry funded clinical trials. Declarations of Col must cover the last three calendar years. Members may use the Col-forms provided by ISDB or their own forms as long as they cover a similar set of questions.

Independent editorial team

Members of the editorial team must be free from Col with the healthcare industry. Their Col-declarations should be updated annually and publicly available.

Organizational structure

a. Institutional setup:

If the publication is part of a larger institution, safeguards must be in place to prevent any influence of the institution (or the governing board of a bulletin if applicable) on the editorial team, particularly regarding topic selection and article content.

b. External authors:

If an editorial team makes use of external authors to write or draft articles:

- The editorial team must have the autonomy to change the content or reject articles.
- All authors who write articles which could influence therapeutic choices (e.g. drug and treatment

reviews or guidelines) must be free from Col as defined above.

- In exceptional circumstances a bulletin may publish an article (not influencing therapeutic choice) by an author who has a conflict of interest; in such a situation all Col need to be declared at the end of the article.

c. Reviewers of articles:

External reviewers of articles should declare their Col.

New website

The new website was launched in the beginning of 2018. We thank our webmaster Alexander Smakman and Siem Looyen. There is still some work to be done and especially related to the updates of the member's organizational data. Therefore, we ask all members, full and associated, to once again check whether their data shown are correctly.

Also, there is now a picture of capsules which is not quite what we would like. Any suggestions for a better one are very welcome.



We have been working hard. Two years ago, we divided *Bulletin Farmacos* in four bulletins. Due to the large amount of information that is emerging and the interests of our Spanish readership, one of the bulletins has been dedicated to Ethics and Clinical trials. The other bulletins are devoted to Pharmacovigilance and Appropriate use, Access and Economics, Regulatory Agencies and Policies. Consequently, we have increased the number of translations into Spanish from English and French sources.

We are presently conducting a study on the role of research ethics committees (RECs) in eight Latin-American countries (Argentina, Brazil, Chile, Colombia, Dominican Republic, Mexico, Panama and Peru). This effort began almost two years ago. *Salud y Farmacos* developed a proposal aimed at uncovering strategies to strengthen the capacity of Latin American to protect clinical trial participants and the integrity of data collected during the trials. There is ample evidence that RECs are unable to protect research participants in clinical trials sponsored by industry. In fact, the RECs do not verify if the subjects have understood the consent form. Also, RECs are told that they cannot even modify the consent form when they complain about translation errors or when the form is too lengthy or too complicated for the research participants to understand. If RECs can't modify the wording in an informed consent, they have

even a harder time questioning the design of the trial, the treatment for the comparator group or the sample size. Under current conditions, well-intentioned and capable RECs have very little decision-making space, they either approve the clinical trial as presented or they reject it. If they reject it, the sponsors have identified commercial RECs that would approve them in a few days, a practice known in Colombia as 'carrusel' (merry-go-round).

The number of clinical trials rejected by Latin American RECs is minimal, and in most countries, research sponsors engage in REC-shopping until they obtain the required seal of approval. In fact, increasingly research sponsors are avoiding RECs that use strict approval criteria and flock towards commercial RECs. The only Latin American country that has outlawed commercial RECs is Brazil. In sum, although RECs have responsibility for protecting the dignity and safety of clinical research subjects, under current circumstances, they are unable to fulfill their mission.

Our study consists of: (1) in-depth interviews with current or previous REC members with experience reviewing protocols financed by the pharmaceutical industry; (2) a self-evaluation tool to be completed by REC members; and (3) focus groups with REC members. The research proposal and research instruments were presented and discussed in November 2016 in Bogota, Colombia, during a meeting with all researchers involved in this

project. We are not aiming at evaluating the performance of the RECs, but at finding strategies to strengthen the ethical review of research proposals sponsored by industry. Therefore, we are only involving respondents that are known for being inquisitive thinkers who take to heart their responsibilities as members or ex-members of the RECs. While we were aiming at 10 in-depth interviews and self-evaluation forms, and one or two focus group per country, it appears that some countries, like Brazil and Colombia, might quadruple that number. In small countries, the number of interviews will be less (4 to 8). In terms of financing, the Universidad del Bosque Colombia secured funding for the fieldwork that is being conducted in four cities (Bogota, Bucaramanga, Cali and Medellin) and for all coordination meetings. *Salud y Farmacos* is sponsoring the operational costs in the other countries. All researchers are donating their time.

The project is advancing in all countries but had a slower start than we had anticipated. Unexpectedly, the RECs of some countries questioned the project and delayed for several months its approval. Currently, two countries have completed the first round of in-depth interviews, and all but two are well advanced in the data collection process. We held our first meeting to discuss interim results last May. We expect to be done with all the fieldwork by the end of this year.

Last year, the Journal of

News from working groups (continued)

Empirical Research on Human Research Ethics published the results of our study in Peru (DOI: 10.1177/1556264617720756). Thirteen clinical trial participants were interviewed to assess if they understood the informed consent, and the rights and obligations that ensue from participating in clinical trials. About half of the respondents signed the consent form without reading it, and most of them did not understand basic concepts included in the informed consent. There was evidence of undue inducement by recruiters, and patients engaged in behaviors that would not only threaten their well-being but also jeopardize the quality of the data collected. For instance, they self-medicated, did not take their medications as directed, and did not inform other physicians they consulted that they were participating in a clinical trial.

Nuria Homedes

News from working groups: Clinical Study Reports

In June 2017 ISDB Committee members and other bulletins interested, participated in a workshop on clinical study reports (CSRs). This two-day workshop was organized by the Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care, IQWiG) in Cologne,

Germany. Beate Wieseler and her colleagues lectured about the framework of these CSRs and we could also practice what we had learned. The participants were very enthusiastic about this experience and the Committee discussed how we could further develop our knowledge. Interestingly, the Cochrane Collaboration was also working on this topic and the Committee and interested members gave input to their proposal on the guidance for including CSR's in their reviews. On the Cochrane Collaboration's website the following information was shared (<http://community.cochrane.org/news/request-comments-draft-interim-guidance-how-decide-whether-incorporate-clinical-study-reports-and-other-regulatory-documents-cochrane-reviews>).

A Cochrane funded (Methods Innovation Fund) project has developed guidance on when to consider regulatory data for inclusion in Cochrane Reviews. Regulatory data includes clinical study reports of trials and other studies, and any other relevant information provided to regulators by trial sponsors. This guidance is interim because Cochrane ultimately aim to provide guidance on how to incorporate this type of evidence in Cochrane Reviews to address reporting bias which distorts much of contemporary literature and may affect the conclusions of an unknown number of Cochrane Reviews. This interim guidance includes a rationale, a section explaining

the triggers for consideration of regulatory data, the results of a survey relevant to current Cochrane practice, and a planned interactive glossary of regulatory terms. The guidance development project was coordinated by (Senior Associate Tutor, University of Oxford, UK) with seven other authors representing CRGs and Methods Groups who expressed an interest in contributing to the project.

Cochrane invited anyone within the Cochrane Community with an interest in addressing reporting bias in studies included in Cochrane Reviews. So, all those working in Cochrane Groups (Centres, Fields, CRGs, Methods), trainers and relevant members of the Central Executive team.

Meanwhile, Cochrane reported that the final guidance was made up and delivered to the Scientific Committee meeting in February 2018. CSC members agreed this data was important in tackling reporting bias. The report's findings were accepted in principle by the committee. However, further consideration of roll out and implementation is required within the main body of Cochrane. We wait for the final documents.

What will turn out for ISDB in not yet clear. Is this the start of an ISDB-Working Group on Clinical Study Reports? In any case it is a topic for the next General Assembly of ISDB in Paris 2019. We will keep you informed.

Changes in membership status:

New Associate Member: NoGracias

The NoGracias Platform is a civil non-profit association, whose ultimate goal is to promote a democratic health system at the service of society, that is, public, sustainable, based on the best scientific knowledge and in which transparency, integrity and equity presides over the actions of all its agents.

The activity of NoGracias began in 2008. Since then its influence is growing in the Spanish health field with about 3 million annual visits to its website,¹ conducting multiple outreach and training activities, and carrying out various campaigns such as 'Pills the fair ones'². This action is based on the cooperative and participative work of its members and supporters as well as a formal and informal network of people and organizations sharing purposes. The ultimate objectives are to mobilize citizens, professionals and institutions, generating informed opinion (based on the best knowledge) and influencing decision-makers and legislators. This way, significant changes will be obtained in the democratic functioning of the science-society-enterprise framework of the health sector.

Since its foundation NoGracias has been financed by private donations, with total independence both from the pharmaceutical industry and any public administration. We



The team of NoGracias and its logo

held five national meetings in different Spanish cities, the last meeting in Oviedo in November 2017 with the participation of 400 people, including lay and health citizens. We have a renewed Board of Directors made up of young professionals and activists and in addition to our new ISDB associate membership, we must highlight the imminent expansion of the organization to Argentina, Uruguay and, soon, Peru.

We consider that we are facing a crisis in the relationship between biomedical science, medicine as an institution, health systems and the society itself. Among the causes of this crisis we propose the following decalogue:

1. Transformation of the common

good that is biomedical scientific knowledge into a commodity.

2. Incorporation of the neoliberal economic ethos and the individualistic search for self-interest in the entire technoscientific system.

3. Existence of incentives contrary to the production of better knowledge.

4. Balanced commercialization of new products and an independent professional practice.

5. Inability of traditional safeguards (science, regulation, professionalism, training, ethics) to guarantee the reliability of scientific knowledge, the quality of clinical decisions

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Changes in membership status:

New Associate Member: NoGracias

and the effectiveness/safety of technologies, including drugs, that reach the market.

6. A deficient understanding on the part of professionals and citizens of the fragile intellectual processes that clinical judgment requires.

7. Interest of health organizations and governments to control and standardize professional practice to achieve economic or political objectives.

8. Loss of ethical and democratic content of professionalism in its aspects of independence, objectivity and accountability.

9. Irrationality of some social expectations in relation to health care, technologies and medical practice itself.

10. Overrating of technologies when looking for levers of social progress.

We are in the approval phase of a document of strategic objectives, where we have identified three major areas of work: knowledge, professionals and citizens. The first objective is the construction of a critical knowledge capable of facing the emerging challenges of the current paradigm: medicalization of life (especially in areas such as care for women, children or mental health), overdiagnosis (in relation to preventive and public health interventions), the structural economic inefficiency of health systems, the serious safety problems or the limitations

of Evidence-Based Medicine to address multimorbidity or end of life.

The second priority for NoGracias is the one that aims to build a critical professionalism. It is necessary to explain the relationships between medical knowledge, economic or corporate power and technologies. Professionals must be attentive because the abusive professional exclusivity in the use of knowledge easily becomes the main ally of the power system. Critical professionalism must flee from any saving temptation. For this, an action of resignation to the power on the part of the professionals is necessary; a rejection of the privileges granted by a system that rewards them very generously for being necessary mediators. The system skillfully uses both professional credibility and the reserve of social trust that medicine retains for its own purposes.

The third area of resistance promoted by NoGracias should be the construction of a critical citizenship in health matters. It is important to understand that health is a value essentially linked to the enlightened ideas of freedom and self-determination. Also, 'disease' is a limitation through which freedom must open its way again. In that objective, the resources of medicine have a very limited effectiveness, especially when faced with the increasingly

prevalent problems linked to aging, chronicity and psychic discomfort. Citizens must lead a new movement for wellness that differs from the obsolete and limited defense of public health. More wellness is not the same as more resources for health care and, often, it can be the opposite. The real problem is that the effectiveness of medicine hits the glass ceiling imposed by the social determinants of health. The existence of this glass ceiling must be recognized by all people, not just professionals. Otherwise, society will continue medicalizing poverty and ignorance, unemployment and job insecurity, obesity, the effects of pollution or an insane food system, climate change and patriarchal and psychological violence. We must investigate together, patients and professionals, how to use knowledge to be emancipatory.

References

1. www.nogracias.eu
2. www.pastillasjustas.org

Actions and Campaigns:

How long is the arm of Big Pharma

How does the pharmaceutical industry influence the European Medicines Agency? Can the organization operate independently? On January 9th 2018, experts discussed these and related questions in the European Parliament. With this event, organized by Wemos and the Confederal Group of the European United Left/Nordic Green Left (GUE/NGL), we aimed to call on the European Medicines Agency (EMA) and the European Commission to consider the added therapeutic value of new medicines before issuing marketing authorization, and to strive for more independent clinical research. The discussions took place before an impressive audience of some 100 interested persons from different walks of life, e.g. political parties, patient advocates, health interest groups, pharmaceutical associations, and journalists. There were two expert panels: the first included experts from European institutions - Martin Seychell (Directorate-General Health of the European Commission), Noel Wathion (Deputy Executive Director of the EMA), and Fergal O'Regan (office of the European Ombudsman). The second panel consisted of Dick Bijl (president of the International Society of Drug Bulletins (ISDB), former general practitioner and former editor-in-chief of the Dutch Drug Bulletin

(Geneesmiddelenbulletin), who spoke on behalf of Wemos, Yannis Natsis (European Public Health Alliance EPHA), and Silvio Garattini (Mario Negri Institute, Milan Italy).

Conflicts of interest in all sectors

Dennis de Jong (Member of European Parliament (MEP)) hosted the panel discussions. MEP Bart Staes, EP-rapporteur on the EMA discharge report in respect of the implementation of EMA's budget for the financial year 2016, began by stating that conflicts of interest exist in all sectors, be it pharma, food, agriculture, tobacco or others. He recalled that, in the case of EMA, their 2011-2012 budget control was not approved but suspended due to their unsatisfactory handling of potential conflicts of interest. Improvements have been implemented since then, which goes to show that the Discharge Committee has an extremely important function, namely to assess the hazard of conflicts of interest, in order to evaluate whether society gets value for money when it comes to medicines.

The system's checks and balances

Noel Wathion stressed that contacts between EMA and pharmaceutical companies are essential for EMA's work; without them, EMA cannot do its work properly. However, it is EMA's duty and responsibility to manage

potential conflicts of interest properly and to ensure that its work remains independent. To achieve this, EMA has a system of checks and balances, e.g. robust design of scientific advice and assessment procedures, peer review procedures, rules of engagement with the pharmaceutical industry, transparency on stated interests of its experts, and transparency of assessment reports, meeting agendas, and minutes. He emphasized that thanks to these procedures, no single person can influence decision-making within EMA.

Since 2016, all clinical data that pharmaceutical companies submit to EMA as part of the Market Authorization Assessment documentation must be published – an important transparency development. Wathion is proud that EMA is the first regulatory body in the world to do so, and he challenges medicines researchers to reassess this data, in order to verify EMA's conclusions.

Martin Seychell (DG Sante)

focused on the fact that European institutions interact continuously with all kinds of groups in society: patient organization, NGOs, academics, national health systems, and yes, also pharmaceutical companies. "They all support us as well

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Actions and Campaigns:

How long is the arm of Big Pharma

as challenge us, and so they should. Such discussions are healthy, and will lead to better systems. But it is important to respect each other's roles and responsibilities, and foster trust in the institutions." DG Sante and EMA continue to improve their transparency, rules and protocols to avoid conflicts of interests and undue influences.

Fergal O'Regan stated that the Ombudsman office has been working with EMA on conflicts of interest and transparency issues for over ten years. The transparency requirements are challenging, but they need to be met, in order to maintain the public's trust in the medicines and vaccines authorized by EMA. He referred to the adaptive pathways mechanism, which states that post-market data on a medicine's effectiveness should be made publicly available and that these data should be used to reconsider market authorization, if need be. This is currently not always the case, which

undermines EMA's credibility.

Law as the starting point

Questions from the public addressed the extensive presence of pharmaceutical industry's experts in EMA's expert panels and their dominant influence in clinical trials, and in EMA's protocols and budget. Wathion remarked that EMA, in its way of working and its financing mechanism, follows the law as determined by the European Parliament. If change is needed, then the law needs to change first. He also challenged the audience to name experts who are truly independent; he claimed that it is a fact of life that most experts are somehow affiliated with the pharmaceutical sector. O'Regan added that the Ombudsman's role is to merely to register declarations of interests, not handle conflicts of interests. Of course, it is essential that people do not put themselves in situations where these interests become controversial or conflicting. This should be monitored closely.

Yannis Natsis (EPHA) kicked off the second panel by reiterating the need for trust in the European Medicines Agency (EMA). He highlighted the need for a critical review of the top EU regulator, which is why he very much welcomed the discussion, describing it as long overdue. He reiterated that although EMA is primarily a technical and scientific body, its decisions have far-reaching economic and policy consequences. He emphasized the need to break down the silos between national medicines agencies, health technology assessment (HTA) bodies and ministries of health. This should guarantee that the public is able to send the right signals to the market, and ask the right questions in the drug approval process - for the benefit of all patients.

Half of new medicines are 'nothing new'

Dick Bijl, on behalf of Wemos, referred to publications on the added therapeutic value of new drugs on the market, citing that only 30% were found to be 'possibly to really helpful', 51% could be described as 'nothing new', and 14% were considered 'not acceptable'. He underlined the importance of independent clinical trials, as they have been proven to consistently yield



Martin Seychell Dennis de Jong,
Noel Wathion and Fergal O'Regan.



Silvio Garattini, Dennis de Jong,
Yannis Natsis and Dick Bijl.

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Actions and Campaigns:

How long is the arm of Big Pharma

clearer results and less false positive outcomes. European politicians should therefore facilitate the legal possibilities for EMA to demand such trials from the industry. Drug trials should focus on direct comparison with existing treatments, instead of placebo-controlled design, which obviously yields more positive results.

Accelerated approval for drugs

Silvio Garattini presented additional information in support of Bijl's statements. He mentioned that accelerated approval has taken place for drugs that had not even reached the Phase III trials stage, meaning that they had not been investigated according to agreed standards of quality, efficacy and safety. Still, they were admitted to the market. He reiterated Bijl's point of view that the need to consider added therapeutic value of new drugs is of direct interest to patients' and public health needs.

His concrete recommendation is to create a renewable fund of at least 1 billion Euros (amounting to less than 0,3% of the EU's pharmaceutical market) for undertaking non-profit independent research. And to possibly learn from the United States, where programs have been set up for trials in which the efficacy of drugs is compared directly. Garattini also pointed out the increasing dependence of EMA on money from the

pharmaceutical industry, these days contributing over 83% to the overall budget, and other ways the industry has a stronger say in EMA policy, which poses a risk for conflicts of interest.

Higher standards are necessary

Questions from the audience fueled the discussion about some interesting points. DG Sante remarked that 'me-too' drugs - medicines that are very similar to existing drugs, and with little to no added therapeutic value - drive prices down, which is positive in itself. However, Garattini believed that by demanding that me-too drugs are better than placebos, the bar is set very, and unacceptably, low. We should demand better than that, as we are basically rewarding pharmaceutical companies for sloppy research by allowing new drugs with hardly any added value on the market. We need to find ways to incentivize the industry to invest in the development of innovative drugs for real and unmet medical needs.

Value for money

Wathion (EMA) remarked that for market authorization to be granted, the data on the benefit-risk-ratio need to be robust; this also holds true for me-too drugs. However, he pointed out that it is the responsibility of national health authorities to decide whether those drugs are reimbursed in their insurance schemes; in other words, to weigh their medical value against their costs. He

again pointed to the possibility of scrutinizing the available clinical data to assess additional criteria of cost-effectiveness.

First steps taken

Wemos and ISDB were very satisfied with the outcome and interest in the event. Because the European Medicines Agency is moving from London to Amsterdam, we should take the initiative to look for ways in which we can improve EMA policy. We hope that this event was a first step of the European institutions to improve legislation in order to prevent conflicts of interest in the best interest of patients' health.

After this meeting the EP adopted on 18 April 2018 regarding EMA's discharge report about the implementation of EMA's budget for the financial year 2016 claims to include 'added therapeutic value' as a fourth requirement for a marketing authorisation:

19. Acknowledges that approvals of marketing authorisation applications are based on three criteria: efficacy, quality and safety; recommends that a fourth requirement should be added: Added Therapeutic Value (ATV), comparing a medicine with the best available drug, instead of comparing it to placebos:

<http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P8-TA-2018-0150+0+DOC+XML+V0//EN&language=EN#BKMD-103>

Corinne Hinlopen (Policy Researcher Wemos)



Meeting in De Balie, Amsterdam: Ella Weggen (Wemos), Dick Bijl (ISDB), Nicholas Freudenberg and Wanda de Kanter (chest physician).

On Wednesday April 25th 2018 Wemos and the International Society of Drug Bulletins (ISDB) organized a meeting in Amsterdam with New York professor of Public Health Nicholas Freudenberg on the disastrous influence of the business community on public health. Other speakers were Wanda de Kanter, chest physician and trigger of the anti-smoking movement, and Dick Bijl, independent drug expert and ISDB President.

In his book “Lethal but Legal” Professor Nicholas Freudenberg describes how tobacco, food, pharmaceutical, alcohol, weapons and automobile industries have a much greater impact on the health of today’s human being than scientists and policy makers with their information and education campaigns.

While the collective influence of these companies has grown, governments are increasingly stepping back and taking decisions that large companies benefit from at the expense of public health. The company’s commitment to profit maximization is associated with the increasing burden of disease and the growing costs of health care.



Nicholas Freudenberg

Freudenberg outlines the image of a modern society that is no longer thinking clearly. First, billions are spent annually to entice people to buy unhealthy products, and then a fraction of this are used to nullify the damage that the world’s most refined marketers have created. Such a public health policy is doomed to failure.

At the meeting, Nicholas Freudenberg discussed the background and problems of this ‘consumer-industrial complex’ and contributed some possible solutions. Wanda de Kanter and Dick Bijl offered reflections from their own expertise. Then a forum debate followed under the

direction of GP Hans van der Linde.

The hold of the medicine sector According to Dick Bijl, the drug market has been flooded with countless medications that do not provide any noticeable benefit to patients and which, moreover, often have many side effects. In the EU alone, for example, around 200,000 people are estimated to die each year due to this, and these deaths are largely avoidable.

Bijl: ‘The pharmaceutical industry has created a situation in which they in fact are the boss of the authorities that approve its medicines and monitor their side effects. Government and politics have accommodated this. They have given up and have been unable to counterbalance the harmful health effects of many medicines.’



“Legal but Lethal”

We believe Cochrane is a key source of scientific evidence on diagnostic and therapeutic medical issues. The very recent expulsion of Peter Gøtzsche from the Cochrane Board and subsequent retirement of four Board members have great impact on the existence of this organisation. Beside issues mentioned by other authors¹⁻³ we believe this crisis is a good opportunity to fix a big problem raised by Peter Gøtzsche and others about Cochrane's conflict of interest policy.

Currently, Cochrane allows some authors of its reviews to have conflicts of interest with drug companies, a policy that is widely criticized by insiders, and largely unknown to the public.

It is well known that researchers with conflicts of interest judge more positively about drug therapies than researchers without such ties. Gøtzsche said that Cochrane's policy regarding conflicts of interest of authors of reviews was inadequate. But Cochrane did not solve this problem. The International Society of Drug Bulletins (ISDB) has criticized this policy already in 2013.⁴

Because organisations like Cochrane play a key role in assessing clinical trials and other evidence regarding medicines, it is essential that they have robust policies with regard to conflicts of interest.

The International Society of Drug Bulletins (ISDB) is a worldwide network of bulletins and journals

on drugs and therapeutics that are financially and intellectually independent of the pharmaceutical industry.⁵ Cochrane reviews have been considered important scientific and trustworthy references for ISDB members. In 2016 ISDB adopted a policy that will be totally implemented in 2019, in which members are not allowed to have conflicts of interest with the healthcare industry. Those who have not fulfilled the criteria will be removed from the full membership list.

A **Conflict of interest** is defined as any financial or advisory relationship (paid or unpaid) with the pharmaceutical industry or related healthcare industry (e.g. medical devices or diagnostics), including the conduct of industry funded clinical trials. Members of the editorial team must be free from conflicts of interest with these industries. All authors who write articles which could influence therapeutic choices (e.g. drug and treatment reviews or guidelines) must be free from conflicts of interest.

What is at stake is the not the transparency of conflicts of interest or whether or not it is feasible to get rid of conflicts of interest it is definitely about **trust, credibility and scientific integrity**.⁶

Cochrane is damaging the trust and credibility doctors, pharmacists, scientists and patients have put in them.

Cochrane's credibility and trust are largely at stake if they do not adequately deal with this issue

immediately.

ISDB therefore supports Gøtzsche's claim that a recovery from this dire situation would call for the dissolution of the present board, new elections and a broad-based participatory debate about the future strategy and governance of the organisation.

1. Demasi M. Cochrane – A sinking ship? <https://blogs.bmj.com/bmjebmspotlight/2018/09/16/cochrane-a-sinking-ship/>

2. Greenhalgh T. The Cochrane Collaboration – what crisis? <https://blogs.bmj.com/bmj/2018/09/17/trish-greenhalgh-the-cochrane-collaboration-what-crisis/>

3. Moynihan R. Let's stop the burning and the bleeding at Cochrane — there's too much at stake. <https://blogs.bmj.com/bmj/2018/09/17/ray-moynihan-lets-stop-the-burning-and-the-bleeding-at-cochrane-theres-too-much-at-stake/>

4. Schaaber J. Cochrane under influence: assessment of the HPV vaccines and conflict of interest. ISDB Newsletter 2013;2:8.

5. www.isdbweb.org

6. Menkes D, Bijl D. Credibility and trust are required to judge the benefits and harms of medicines. BMJ 2017;358:j4204.

Dick Bijl, president International Society of Drug Bulletins (ISDB), on behalf of the ISDB Committee: Luis Carlos Saiz Fernandez, Maria Font, Ciprian Jauca, Christophe Kopp, Benito Marchand, Joerg Schaaber.