

## ISDB 2017 Update of activities and Newsletter

Welcome to the ISDB newsletter of 2017. We report summaries of the General Assembly in Pamplona, Spain in 2015 and the Extraordinary General Meeting in Leiden, the Netherlands in 2016. The minutes of the meetings of the ISDB Executive Committee held in Leiden 2016, Amsterdam 2017 and Cologne 2017 will be put on the ISDB website on the members-only section.

A new website is under construction and we hope to present it in the coming months.

The most important change is to the ISDB policy on *conflict of interest*. This was agreed at the Extraordinary General Assembly Meeting in Leiden 2016. The message is clear: ISDB does not accept that members or editors of editorial Committees have any conflicts of interest. This policy decision is to be implemented immediately. Recently, a letter regarding this new policy was mailed to all members.

ISDB co-founder Andrew Herxheimer died in 2016 and Etzel Giesling (Pharma-kritik) remembers Andrew on page 5 and 6.

Belgian liberal Minister of Public Health puts an end to Belgian full ISDB membership (page 6). On June 30th the Dutch Geneesmiddelenbulletin 2016 organized a Symposium called 'Science and economy' to which all ISDB and associated members were invited. A short report of the meeting is presented on page 7. Finally, an editorial by David Menkes and Dick Bijl on conflicts of interest that was published in the BMJ is presented on page 8.

**The next newsletter is planned for Spring 2018. We welcome suggestions and articles. Please send them to: [president@isdbweb.org](mailto:president@isdbweb.org)**

The Committee wishes you a happy New year and best wishes for all!



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# General Assembly Pamplona 2015, June 28 - July 1

The General Assembly (GA) 2015 was hosted by the 'Boletín de Información Terapéutica de Navarra' (DTB Navarra). Attendees were welcomed to the Assembly and Pamplona by Juan Erviti, chief editor of Bit Navarra and ISDB President Jörg Schaaber. The GA took place in the Instituto Navarro de Administraciones Públicas.

The morning sessions on June 28th were dedicated to accelerated approval procedures in the EU and Canada (the adaptive licensing procedure) with inspiring talks by Teresa Alves and Joel Lexchin.

The problem of conflicts of interest was initiated by Katrina Perehudoff from the European Consumer Organization BEUC. She talked about conflicts of interest at institutional level.

In the afternoon there were several workshops: sustainability and continuing medical education; why and how to develop a subscription-based bulletin; and how to evaluate a bulletin. The last item was especially important as the ISDB Committee is about to conduct another round of bulletin evaluations.

On Monday there was an interesting talk by Tom Jefferson of the Cochrane Collaboration on RIAT, an initiative aimed at Restoring Invisible and Abandoned

Trials. Tom also shared his experience with access to unredacted clinical study reports (CSRs). CSRs contain the raw data of clinical trials and some are available for analysis by independent researchers. A good example is study 329 on paroxetine and imipramine for the treatment of major depression in children and adolescents. Independent analysis of the data by RIAT yielded far less positive effect on efficacy and also raised more doubts about potentially severe adverse-effects.

In a combined talk Peter Gøtzsche and Barbara Mintzes showed how to get hold of clinical data from regulatory agencies and what to do with it. The antidepressant vortioxetine was chosen as a case study. This drug was approved for marketing in the US based on the subset of trials that had a positive result on efficacy on at least one primary outcome (6 of 10 submitted short-term RCTs). Results of negative or neutral trials were ignored, except in relation to harm. The EMA approved vortioxetine based on a judgment that efficacy was established for at least one dose level in 9 of 12 studies. In both cases, the required level of efficacy was low and not necessarily clinically relevant.

In the afternoon other workshops took place namely one about drugs to avoid.



Peter Gøtzsche in Pamplona.

The last item of the agenda was dedicated to the conflict of interest policy. These were lively discussions as the opinions of the bulletins being represented were quite diverse. Although the initial intention was to vote on the proposed rules, the assembly could not reach an agreement. It was decided that further discussion and the subsequent voting would be postponed until the following year, 2016. An Extraordinary General Meeting was to be held in the Netherlands during the 50th anniversary of the Dutch Geneesmiddelenbulletin. Meanwhile, the ISDB Committee was expected to keep on serving for one additional year.

In the evening Peter Gøtzsche presented a very interesting talk about overdiagnosis and overtreatment with psycho-active drugs in psychiatry and also introduced his new book "Deadly Psychiatry".

Closing remarks were spoken by the Minister of Health of the Government of Navarra.

The morning of the last day included a workshop on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) facilitated by the Canadian group Therapeutics Initiative.



Group photo at the General Assembly in Pamplona (©2015, J. Schaaber).

# Extraordinary General Meeting Leiden 2016, July 1 - 2

On Thursday June 30th a welcome dinner took place in Leiden where ISDB members had the opportunity to meet each other.

The EGM took place at a very special place: the old Hortus Botanicus of Leiden University.

On Friday July 1st the president introduced the meeting and ISDB members shared memories of co-founder Andrew Herxheimer who had died on 21st February 2016 (see also page 7 and 8).

Sidney Wolfe (Worst Pills Best Pills) discussed current problems with the FDA.

Later that morning Teresa Alves talked about the EMA's Adaptive pathways project. The afternoon session dealt with the debate on the proposed ISDB Conflict of interest (Col) policy. Jörg Schaaber started by presenting the ISDB rules on this topic. Then a panel of speakers discussed the pros and cons of allowing external authors



Sidney Wolfe in Leiden.

with Col: Giampaolo Velo, Focus, Italy (absent due to illness), Christophe Kopp (Prescrire, France), Wolf-Dieter Ludwig, (Arzneimittelbrief, Germany) Frans Helmerhorst (Geneesmiddelenbulletin, The Netherlands). The discussion was moderated by David Menkes.

On page 4 the new ISDB rules of Col are presented.

There were two workshops: 'Access to

data (how to get it and what to do with it?)' facilitated by Gianni Tognoni and 'Drug regulation and transparency for patients and prescribers' facilitated by Teresa Alves.

Saturday July 2nd started with a short history of the Geneesmiddelenbulletin by Dick Bijl. Then Allen Frances talked about Benefit and harm of antidepressants and how to communicate about sensitive topics against the mainstream.

The results from workshops were presented in plenary and the voting on Col rules took place (page 4).

Once the new Committee was elected and appointed the Meeting was closed and the new Committee met for the first time.

The presentations shared at this meeting will be made available on the ISDB members-only website. The presentations from the 50th anniversary symposium are already available on-line on: [www.geneesmiddelenbulletin.nl](http://www.geneesmiddelenbulletin.nl)



EGM in Hortus Botanicus, Leiden University, The Netherlands on July 2nd, 2016.

# Conflicts of interest

The conflicts of interest (Col) amendment was discussed. The President introduced the theme for discussion. Proponents and opponents of the amendment to the ISDB rules had the opportunity to present their views. The final wording of the amendment was put forward for approval and read as follows:

## ISDB EGM 2016: Proposed clarifications of CoI policy

### *New rule V: Definition of Independence*

The following definitions refer to the requirements of independence of a bulletin (Article 2)<sup>1</sup> and the independence of the editorial process (Article 4.1.1)<sup>2</sup> and specifically address conflict of interests (Col). This rule was established at the Extraordinary General Meeting (EGM) 2 July 2016 in Leiden. It applies immediately on new ISDB members. Existing members will be entitled to a three-year transition period to comply with the provisions of the rules, as described below.

#### **1. Definition: Conflict of interest (Col) 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.

#### **2. Independent editorial team**

Members of the editorial team must

be free from conflict of interest (Col) with the healthcare industry. Their Col declarations should be updated annually and publicly available.

### **3. 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 conflict of interest 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.

#### **1. Article 2 [...]**

“Independent”: A publication is independent if it fulfils the following three criteria:

- a) it is run by an independent editorial team;
- b) its organizational structure and financial resources are capable of guaranteeing the editorial team's independence;
- c) it does not accept any funding from the pharmaceutical industry or related healthcare industry.

#### **2. Article 4.1.1 [...]**

- that they shall allow the quality of the bulletin and the independence of their editorial system to be periodically assessed by the Society;
- that they will inform the Committee of any changes in structure, working, financing or editorial organization likely to modify their independence or the quality of their content.

The vast majority of EGM participants also decided to vote immediately on the amendment as they felt that there was no reason to postpone the voting to July 2nd.

Prior to the procedure, the President confirmed that the Meeting reached

the quorum to proceed with the voting. Carlos Durán (observer and not an ISDB member) collected the votes. He also counted them with the help of Hedwig Diekwisch, sociologist working at the German ISDB-journal Buko Pharma.

The results obtained were as follows:

YES:	25
NO:	3
ABSTENTION:	1
TOTAL VOTES:	29

Therefore, the amendment proposal was adopted for further enactment.

# New ISDB Executive Committee

On July 2nd, the election of new Committee members took place. According to the ISDB Constitution, the minimum number of members should be 5 and the maximum 11. The President and General Secretary suggested that the number of members elected should be reduced to 7, since this is sufficiently large to address all the Committee's undertakings, and if larger, the economic burden of the Committee meetings increases notably. Discussion ensued and the meeting voted and approved the proposal to reduce the number of Committee members to seven.

There were 13 candidates for the seven places on the ISDB Committee. The candidates shared their reasons to join the Committee. For those candidates who were unable to attend the meeting, another member spoke on their behalf.

## New ISDB Committee

The 7 elected members of the new Committee were:

- Ciprian Jauca (Therapeutics Initiative, Canada)
- Christophe Kopp (La Revue Prescrire, France)
- Luis Carlos Saiz (DTB Navarre, Spain)
- María Font (Infofarma, Italy)
- Benoit Marchand (Yachay, Ecuador)
- Dick Bijl (Geneesmiddelenbulletin, The Netherlands)
- Jörg Schaaber (Pharma-Brief, Germany).

According to the ISDB Constitution, Committee members are appointed for a three-year term. However, as this was an Extraordinary General Meeting it could be interpreted that because the last ISDB GA took place in Pamplona in June 2015, the Committee elected in Leiden would only serve for two more years.

It was widely accepted that a two-year mandate is too short to implement any relevant change in the ISDB. It was decided that the Committee members will serve until the General Assembly in 2019.

## ISDB EXECUTIVE COMMITTEE MEETING Leiden, the Netherlands, 2nd July 2016

### *The new Executive Committee*

After closing the EGM the new Committee held its first meeting in order to elect the new President, General Secretary and Treasurer as well as to establish the roadmap for the next months.

The following was decided:

- Dick Bijl – president
- Ciprian Jauca – secretary
- Luis Carlos Saiz – treasurer

### *Responsibilities*

Jörg Schaaber and BUKO will continue to be responsible for the accounts.

Dick Bijl has offered to assist with the website.

Maria Font will be responsible for keeping the members' records up to date.

# Remembering Andrew Herxheimer

## *Etzel Giesling, editor, pharma-kritik*

Andrew Herxheimer, initiator and co-founder of the International Society of Drug Bulletins, died on 21 February 2016 at the age of 90. His great merits have been honoured in so many obituaries that it is impossible to add anything of general importance. I would therefore like to restrict myself to personal memories - if you want to watch video recordings of a memorial meeting or read a selection of obituaries, you can find the corresponding links at the following address:

<http://pkweb.ch/2wpROIb>

Andrew was one of the first to recognize the importance of independent drug

information and implement it with appropriate projects. I don't know if I would have dared to launch a similar publication (pharma-kritik) for Switzerland without the model of his Drug and Therapeutics Bulletin. Andrew himself encouraged me to take the plunge long before ISDB existed. So it was self-evident that we both worked in the first ISDB Committee, discussed the necessary structures and considered desirable liaisons with related organisations. Andrew as president has shaped many ISDB features, although there has been some controversial debate in our Committee meetings on details. In the first few years, the Committee convened most often in European cities, mainly Paris or

London, but also in Prague, Berlin and once Zurich. Andrew, the fluent linguist, was able to get his point across in many cases, all the while being a loyal discussion partner on controversial topics. I was always impressed by how modestly he appeared and how well he could bring a humorous note into difficult conversations.

Even though we met the Herxheimers on official occasions only, my wife and I found Christine and Andrew to be real good friends. After the meetings, which were quite often demanding, it was always a pleasure for us to meet them in the evening, together with the small circle of Committee members. We often heard about the many other tasks

## Remembering Andrew Herxheimer (continued)

and initiatives that Andrew brought to the most different continents. Andrew is remembered to me as the best example of a creative person; so it is not surprising that he remained active, interested and committed until old age. Much later, when we were both no longer on the ISDB Committee, I met him several times at the Pilule d'or meetings organised by 'La Revue Prescrire' and was impressed every time by how well he was informed about all medication issues and how brilliant his puns had remained.

**ISDB has decided in the Extraordinary General Meeting in Leiden 2016 to hold a "Andrew Herxheimer Memorial Lecture" at each General Assembly to honour his merits for independent information.**

Among all the drug letters I know, I remember the issues of the Drug and Therapeutics Bulletin produced under Andrew's leadership as a model for critical yet balanced information. Of course, I regretted that according to UK law he had to resign as an editor in 1992, too early in my opinion. Since then, there have been many changes in the DTB - not always to the advantage of this publication, although it remains worth reading today. Of course, the extraordinary significance of the DTB in the 1970s and 1980s is not based exclusively on Andrew's specific know-how. Those years were also marked by innovations that had a greater impact on our daily practice than today's new product launches of highly specialized active ingredients.

Thanks to his linguistic brilliance, Andrew had the ability to effectively highlight characteristics relevant to patients. He then passed on key elements of this knowledge in various ISDB events and courses, thus improving ISDB publications in other countries.

With Andrew's death, the independent drug information will not disappear. With him, however, we have lost an unusually committed and innovative colleague. His influence will undoubtedly continue to be felt in the future.

*Etzel Gysling (Editor, pharma-kritik)*



Presentation of the ISDB manual on Starting or Strengthening a drug bulletin, Melbourne September 12th 2005 with a proud and happy Andrew Herxheimer in the middle.

# Belgian liberal Minister of Public Health puts an end to Belgian full member of ISDB

Starting 3 years ago as a minister, Maggie De Block, a general practitioner, member of the liberal Party, promised a policy, based on EBM. At this moment, she realized three times the opposite of what she promised.

Instead of promotion of all organizations of EBM, she gives orders to spare 30% of the budget. At the other side, Belgium scores very badly in terms of over-prescription of antibiotics and psychoactive drugs. Therefore, she advances the price for the patients: nevertheless, doctors prescribe antibiotics.

Secondly, she stopped completely the subsidy for one project: The Educational Outreach visits. This was part of the project Farmaka, founded in 1979. This organization published a 'Medical Drugbook' (1983) contenting a commented selection of 150 drugs for the general practitioner. At this moment, two projects were realized: a Formulary

for treating old patients, and the Educational Outreach visits, started 20 years ago: one of the first initiatives in Europe. This face-to-face strategy is very effective and can save money on the long term.<sup>1</sup> Representatives of different organizations came to Ghent (Belgium) to study the training of the visitors and the implementation of this strategy. This year, 5000 GP's were visited: 95% asked to continue these visits. This project is obliged to stop on January 1<sup>st</sup> 2018: 15 independent visitors (mostly part-time) are being dismissed. Nevertheless, one of the slogans of the government is 'jobs, jobs, jobs'. Because this project was the most important of the project Farmaka, it will be the end of this organization, after nearly 40 years. Farmaka was one of the founders of the ISDB in 1986.

Last but not least. The minister ordered the end of this project, some months before the publication of a report on the needs and the organization of all EBM-

organizations. This report is prepared by the Belgian Health Care Knowledge Centre. In this way, the minister made her conclusions before the report will be published. This is a form of political influence that is inadmissible.

This policy of the minister is a gift to the pharmaceutical industry which continues to send some thousands 'dependent visitors' every day to the doctors. Tomorrow we will have higher over-prescription of antibiotics and psychoactive drugs, with thanks to the minister of Public Health.

1. Chan WV, et al. Special Report: Clinical practice Guideline implementation Strategies. A summary of Systematic Reviews by the NHLBI implementation Science Workgroup. *J Am Coll Cardiol* 2017;69:1076-92.

*Marc De Meyere*

## Symposium 50th anniversary Geneesmiddelen-bulletin

**Leiden, The Netherlands, June 30th, 2016**

On 30 June 2016, Geneesmiddelen-bulletin celebrated its fiftieth anniversary by organising a symposium entitled 'Science and Economy', about the role of the pharmaceutical industry in scientific research. Industry-sponsored studies are increasingly presenting an overly favourable picture of the efficacy and side-effects of medicines. This practice does not always benefit science, nor the patients. The speakers at the symposium analysed the problem and tried to suggest solutions where possible). The presenter of the symposium, Richard Smith, is well familiar with the subject. Until 2004, Smith was an editor at the

British Medical Journal (BMJ), and in 2006 he published a book entitled *The Trouble with Medical Journals*, in which he showed how medical science media were in danger of becoming the spokespersons of the pharmaceutical industry.

In recent decades, the Dutch government has deliberately promoted intensified collaboration and integration between business and universities. Many have claimed that this collaboration offers major economic advantages and will enable us to overcome the huge economic and social problems we will be facing.

However, the influence of trade and industry and the relations between business and science have come under increased scrutiny, especially as regards the question whether this relation has yielded positive or negative health effects. The discussion involves political, social, economic and scientific aspects. At the symposium, the debate focusses on rational pharmacotherapy.

Nicholas Freudenberg, Professor of Social Epidemiology in New York, discusses the influence of trade and industry on health. Based on his book *Lethal but Legal*, he demonstrates the similarities between six major industries

## Symposium 50th anniversary Geneesmiddelenbulletin (continued)

(the food industry, the tobacco industry, the pharmaceutical industry, the alcohol industry, the car industry and the arms industry). These industries have a much larger influence on human health than the decisions made by scientists and policy makers. Whereas the collective influence of these industries has grown, many governments have gradually reduced their involvement and have also taken decisions that benefited the industries at the expense of public health. The industries' profit maximisation efforts have been associated with the increasing burden of chronic diseases and disorders, as well

as the growing health care costs.

Other topics to be discussed in the morning programme include the entrepreneurial university, medicalisation, drugs as major causes of death, bias in drugs research, threats to scientific integrity and the role of drug bulletins.

The afternoon programme was devoted to psychiatry and psychiatric drugs. Psychiatry is the area of medicine characterised by the greatest controversy about the importance of diagnostic classifications, medical

treatment and the meaning and interpretation of research findings.

The symposium enabled the audience to critically consider the role and influence of the pharmaceutical industry, as well as their own activities. Many of them left the conference hall determined to be more reticent about prescribing drugs, particularly psycho-pharmaceuticals, and having become aware that symptoms that appear after the use of a drug is discontinued do not stem from the presence of a disease, but are in fact withdrawal symptoms.

# Letter: Credibility and trust are required to judge the benefits and harms of medicines

## Published in *BMJ* 2017;358:j4204.

Freer and Godlee<sup>1</sup> consider the serious doubts held by both the public and the profession regarding drug efficacy and safety, and lament the weak recommendations made by the Academy of Medical Sciences to address the fundamental problem of conflicts of interest (Col) in drug information.<sup>2</sup>

Since medical journals play a key role in accessing clinical trial and other evidence regarding medicines, it is essential that they have robust policies with regard to Col. Unfortunately, progress in this area has been inconsistent, with some prominent journals having recently taken a more 'flexible' view regarding conflicted authors.<sup>3</sup> The International Society of Drug Bulletins (ISDB) is a worldwide network of journals that operate independently, both financially and intellectually, from the pharmaceutical industry. Founded in 1986 with the support of the WHO Regional Office for Europe, ISDB's rationale is that drug bulletins without industry funding avoid

problems faced by editors of other journals, for example in reporting the results of sponsored drug trials.<sup>4</sup>

Financial conflicts are, however, not the whole story, and ISDB has continued to debate its policies regarding Col.<sup>5</sup> At a recent extraordinary general meeting, ISDB members voted overwhelmingly to further strengthen the Society's policy on Col, defined as any financial or advisory relationship (paid or unpaid) with the pharmaceutical industry. ISDB decided that its editorial teams and external authors influencing therapeutic choices must be completely free from Col. This policy change reflects the accumulating evidence of bias arising from both financial and advisory links with industry, as well as the recognition that disclosure of Col is often inadequate and may, under some conditions, even aggravate bias.<sup>6</sup> While trust in doctors is largely determined by our perception of their knowledge and experience, credible drug information requires that Col are not merely managed but effectively excluded.

1. Freer J, Godlee F. Judging the benefits and harms of medicines. *BMJ*. 2017;357.
2. Academy of Medical Sciences. Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines. 2017 <https://acmedsci.ac.uk/file-download/44970096>.
3. Godlee F. Conflict of interest: forward not backward. *BMJ : British Medical Journal*. 2015;350.
4. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *BMJ*. 2003;326(7400):1167-76.
5. Menkes DB. Conflicts of interest and drug information. *BMJ*. 2011;343.
6. Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure.

**JAMA. 2012;307(7):669-70.**

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