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ISDB 2020 COVID-19 Special Edition Newsletter

Remarks from Dick Bijl, Chairman of ISDB


Dick Bijl, Chairman of ISDB
(Photo by Jörg Schaaber)

Dear friends,
This first newsletter of 2020 has us focusing on the current pandemic through a selection of articles by our members and associated members. Right from the beginning there were many claims being made that certain drugs were helpful in treating patients. But as we know documenting many of the problems drug bulletins have to contend with, there were problems with this research: lack of control-groups, too short follow-up, lack of reporting on hard clinical endpoints, or only reporting surrogate endpoints, and poor evaluation of side effects and adverse events. At this moment in the database of the Food and Drug Administration, clinicaltrials.gov there are 551clinical trials actively recruiting patients for COVID-related studies, most of which are examining some aspect of drug therapies for Covid-19. Most trials hardly add anything to our knowledge of treatments but do cost much energy, time, money and good will of doctors and patients.

The statement ISDB made and circulated by social media and through our website stresses the importance of thorough, trustworthy clinical trials before judging that certain drugs and vaccines are efficacious. Randomised clinical trials are the only way in which efficacy can be proven. You will find our statement on the website.

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General Assembly Paris

From 10-12 October 2019 La Revue Prescrire hosted the General Assembly in Paris. We were happy to welcome a total of 29 full and associate members with over 50 participants. Two new associated members organisations introduce themselves, Farmaco-logico from Italy and Pharmed-Out from the United States of America.

Thursday morning was dedicated to internal ISDB-affairs. Dick Bijl gave a summary of the activities of the Committee. Apart from Committee meetings, working groups and advocacy groups, the quality of publications of full members was assessed. The Conflict of Interest policy as adopted in Leiden 2016 was implemented. We learned of collaborations with Wemos in the European Parliament and Meduwa in water pollution. We discussed press work, external communication and collaboration and recruitment of new members, and checking of membership status.

ISDB Membership

A call for new Committee-members was held as 4 members intended to leave the Committee. Jörg Schaaber (Pharma Brief, Germany), Christophe Kopp (La Revue Prescrire, France), Ciprian Jauca (Therapeutics Initiative, Canada) and Benoit Marchand (Excellencis, Ecuador) had been part of the Committee for many years.

Thereafter, Luis Carlos Saiz gave a summary of the financial matters and the membership subscription status and were complemented for their excellent work. ISDB had 35 full members and 24 associated members. New members introduced themselves. Maria Aldunate from Chile (Boletín Farmacovigilancia), Carlos Duran from Ecuador (Excellencis-Ecuador) and Gopal Dabade from India (DAF-K). David Healy from Canada (RxISK.org) and Abel Jurado from Spain No-Gracias joined later. Unfortunately, ISDB had to say farewell to 10 organisations.

Maria Font (Infofarma, Italy) gave a summary of the quality-check of full members. Every few years the Committee reviews the quality of articles published in the bulletins or the websites according to a checklist. She concluded that the quality of the bulletins was good and all members complied to the rules.

Conflict of Interest Policies

After this Dick Bijl gave a summary of the implementation of the conflict of interest policy that was adopted in Leiden 2016. Almost all organisations had implemented the new policy and those who hadn't were kindly asked to submit the necessary document at the assembly.

The previous ISDB Committee Dick Bijl, Ciprian Jauca, Maria Font, Christophe Kopp, Jorg Schaaber, Benoit Marchand, Luis Carlos Saiz (Photo by Jörg Schaaber)

Conflicts of interest jeopardize the integrity, trustworthy and credibility of science and especially pharmacotherapy and drug studies.

Since the General Assembly in Vancouver in 2012 ISDB has been working on a policy to deal with conflicts of interest. In 2015 in Pamplona preparations were made for a policy that was finally approved In the Extraordinary General Meeting in Leiden 2016.

Conflict of interest with the healthcare industry is defined as 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. ISDB finds it necessary for full members to have an independent editorial team. Members of the editorial team must be free from conflict of interest with the healthcare industry.

We have taken a major stance on this issue. ISDB is the first global independent organisation that provides information on drugs and medical devices that are completely free of conflicts of interest, which should be regarded as a landmark. Our next steps will be to implement the policy on the websites of the full members and then make decisions on the way in which the associated members conform to the new policy.

Website Update

The update of the website is almost completed. Members were asked to check their contact-details.

Nuria Homedes (Boletin Farmacos, USA) gave an update of the Clinical trials working group that is operating in North, central and South America. Rita Kessler (La Revue Prescrire) gave some insights on the status of the debates on the proposed Regulation on Health Technology Assessment in the European Parliament and ISDB lobbying activities in this respect.

Finally, Barbara Mintzes (Therapeutics Initiative and University of Sydney) gave a lecture in which she compared the post-market safety warnings of FDA, MHRA/EMA, Health Canada and TGA.

Drug regulatory environment, quality of the evidence needed

The first panel discussion entitled "Drug regulatory environment, quality of the evidence needed" was extremely controversial. While for Jordi Llinares of the European Medicines Agency, (EMA) the world is largely in order, other speakers saw it differently. Claudia Wild of the Ludwig Bolzmann Institute, which is responsible for medicinal products in Austria, pointed to the example of cancer drugs. She noted that far too little is known about the benefits of the drugs at the time of approval and what knowledge is known is not exactly conclusive. If you look at the criteria of the European Cancer Society, only one in five to ten medicines shows a clinically relevant benefit, she said. Over time, the quality of studies is also getting worse and worse. More and more often, surrogate endpoints such as progression-free survival (PFS) would be measured instead of actual survival. This does not benefit patients.

ISDB President Dick Bijl and Sidney Wolfe of Worst Pills – Best Pills from the USA denounced the shamefully low standards for the approval of antidiabetic drugs. Sotagliflozin was only approved by the U.S. regulatory authority as an adjunct therapy for type 1 diabetes: the consultation of the experts ended in a stalemate. The EMA, on the other hand, gave the drug the green light in April 2019, although it was clear that there was a high risk of ketoacidosis – a threatening acidification of the blood – according to Sidney Wolfe.

Sanofi did not initially put the drug on the market despite the approval. In June, new data was announced: sotagliflozin worsens kidney function. On July 26, 2019, Sanofi announced the end of its collaboration with Lexicon, which had originally developed the active ingredient. It was justified on the basis of disappointing efficacy results.

Sotagliflozin had received a normal approval from the EMA. Sanofi was only ordered to conduct a study on the frequency of ketoacidoses. Llinares, on the other hand, defended the EMA's accelerated provisional approval, even if there was weak or incomplete evidence. In his opinion, this was not a problem, as only one of the approved products had to be withdrawn from the market (two other producers withdrew their application for authorization "for commercial reasons").

In most of the rapid approvals, even after several years, it is still unclear whether and what actual benefits the drug might have for patients.

In general, the debate showed that there is a significant gap between the thinking of the regulatory authority on the one hand and independent drug evaluators as well as clinically active doctors on the other.

While the agency is satisfied with statistically significant results, independent experts question whether what counts for patients has been measured at all and whether the treatment also leads to relevant improvements. Another point of contention was the fact that around 90% of the EMA is financed by industry fees. Llinares emphasized his independence, that he gets his salary, whether his agency makes positive or negative about a drug's approval. What he failed to mention is the simple fact that if the EMA were to make stricter judgments, the number of applications for authorizations would be reduced, and thus also reducing the authority's revenue stream. After this the Andrew Herzheimer Memorial Session was dedicated to Evidence-based deprescribing: a challenge for independant drug bulletins.

Benoit Marchand, Sid Wolfe, Martin Canas (Photo by Jörg Schaaber)

Conflicts of interest (CoI) and elaboration of trusted evidence: the way forward

Conflicts of interests still play an underestimated role in medicine. Zoé Friedmann from the Berlin student group of Universities Allied for Essential Medicine (UAEM) offered a refreshing introduction to the topic. She advocates independence in teaching and noted that sometimes professors will put certain drugs in the foreground in lectures without disclosing their conflicts of interest. UAEM investigated in a small study how German medical faculties deal with the problem. The result is sobering to say the least.

Also discussed was the troubling topic of the independence of the Cochrane Collaboration. Last year went through a very painful period in its history when it relieved one of its founding members, Peter Gøtzsche from his duties and excluded him from the group.

His "offence" was that he had deep criticisms of the way Cochrane was handling the conflict of interest issue, leading sometimes to problematic reviews. Juan Erviti from Pamplona, one of the coordinators of the Cochrane Hypertension Group – one of the groups that takes conflicts of interest very seriously – described the handling of data distorted by influence. He also reported that the scandal surrounding Peter Gøtzsche had already changed a lot. Cochrane would be tightening its conflict of interest rules in the future. The ensuing discussion showed that these changes didn't go far enough and Peter Gøtzsche, discussed his newly founded Institute for Scientific Freedom.

Dinner with ISDB Members David Healy, Dee Mangin, Natalie Marti, Juan Erviti, Christophe Kopp (Photo by Jörg Schaaber)

Announcing Two New Associate Members Pharmed Out

PharmedOUT.ORG

PharmedOut is a Georgetown University Medical Center project based in Washington, DC that promotes evidence-based prescribing, educates health care professionals about pharmaceutical and medical device marketing practices, and provides access to unbiased information about therapeutics. PharmedOut investigates the influence of pharmaceutical and medical device marketing on the practice of medicine, and provides access to industry-free continuing medical education (CME). We are also the only group in the world studying industry influence on CME. We are also one of the only groups that investigates industry-invented conditions, including hypoactive sexual desire disorder (HSDD), low testosterone (low-T), binge-eating disorder (BED), and gastroesophageal reflux disease (GERD). In a joint effort with the George Washington University Milken Institute School of Public Health and the Washington, DC Department of Health, we launched The DC Center for Rational Prescribing (DCRx) and created 16 CME courses that are publicly available. As a result of DCRx, Washington, DC became the first jurisdiction in the United States to provide its own evidence-based continuing education for physicians, nurses and pharmacists.

PharmedOut was founded and is led by Adriane Fugh-Berman, MD a professor in the Department of Pharmacology and Physiology and the Department of Family Medicine at Georgetown University Medical Center. The project was originally launched in 2007 with two years of funding from the Attorney General Consumer and Prescriber Grant Program, using funds from off-label promotion of Neurontin (gabapentin). Since then, PharmedOut has been primarily funded by individual donations. Every month, we produce and distribute an electronic newsletter with news, resources, and a monthly column on opioids, to more than 3000 subscribers. In addition, PharmedOut hosts a pharma-free and self-funded biennial conference covering industry influence on medical discourse, >>

Two New Associate Members (continued)

the real risk of prescription drugs, opioids, and other topics.

PharmedOut's website provides open-access slideshows, videos, other educational tools, and a portal to over 150 free, continuing education courses provided by government and other industry-independent entities.

Farmaco-logico, a new way to disseminate independent drug information in Italy

In daily practice it is complex to have access to independent high-quality information, both for the plethora of information and for the intrusion of commercial interests disguised as information.

In the past in Italy, in the field of high-quality independent information, drug bulletins of the ISDB network have distinguished themselves with some excellent publications.
But today the Italian situation of independent information is dire and, after the recent closure of Informazione sui Farmaci, only Ricerca&Pratica and the online version of Infofarma survive.

For this reason, with the aim of increasing visibility and access to independent international bulletins and the best information available from international newsletters, we started Farmaco-logico bulletin. In November 2017.

It's an index to the best free-access articles derived from the international bulletins around the world. The index contains a link to the article, which can be consulted in the original language (English, Spanish, French) and with each issue, a specific drug is described and simplified through an infographic.

In the first three years of activity, the bulletin, published every 4 months, has dealt with the Depakin scandal, the abuse of psychiatric drugs, the waste of resources caused by the excessive prescription of vitamin D, and many other commonly used drugs in general medicine.

Since the last issue, which focuses on the antidepressant withdrawal syndrome Farmaco-logico has become an associate member of the ISDB network.

Here you can download the last number of Farmaco-logico:
http://www.farmacologico.it/il-bollettino/

Enjoy the reading!
Farmaco-logico team

Member Updates on the COVID situation

1. Prescrire and Prescrire International (France) has posted articles related to masks, cleaning and sanitizing and the predictive value of diagnostic tests. Link here

   New data on the cardiac adverse effects of the combination of hydroxychloroquine (Plaquenil°) with azithromycin (Zithromax° or other brands). Link here

   Covid-19 and hydroxychloroquine (Plaquenil°): new data show no evidence of efficacy. Link here

2. Arznei-Telegramm (Germany) SARS-CoV-2: Should you discontinue ACE inhibitors and sartans?" Link here

3. Drugs and Therapeutics Bulletin (UK)
   Deprescribing in the time of COVID-19

4. Therapeutics Initiative (Canada). Pill splitting is one way to stretch prescriptions.
   See our letter here: English. French. Spanish.
   Therapeutics Initiative wrote this statement about the need for randomized trials for COVID-19.

5. Australian Prescriber (Australia) COVID-19 and the quality use of medicines: evidence, risks and fads.
   Link here

6. Med Check (Japan). April 2020 newsletter. Link here

7. NTB Navarre COVID-19: Chloroquine and hydroxychloroquine as potential therapies against COVID-19.
   Link here

Update on ISDB's Clinical Trials Working Group

Report by Núria Homedes

ISDB General Assembly, Paris, October 10, 2019

Abstract: Most regulatory agencies conduct clinical trial (CT) site inspections, but the experiences and behaviors of research subjects and their knowledge of the rights and obligations that ensue from participating in a CT are seldom explored. The authors assessed the technical feasibility of incorporating interviews with participants in CT inspections. This article analyzes the responses of 13 CT participants, 14% (n = 96) of those included in three tuberculosis (TB) CTs. Participants did not object to being interviewed and provided information not obtained during regular inspections. Participants were appreciative of the agency's concern for the integrity of the CT process. Most interviewees did not understand the consent form and were unaware that they were participating in an experiment with unapproved new drugs. Participants' decision to enroll in CT related to undue inducement and therapeutic misconception. Some patients' behaviors, undisclosed to researchers, could have compromised the integrity of the data collected and exposed participants to unnecessary risks (used emergency rooms without informing the attending physician that they were participating in a clinical trial, self-medicated – with pharmaceuticals and/or traditional medicine- manipulated the dosages of the products used in the clinical trial).

Strengthening research ethics committees that evaluate clinical trials sponsored by industry. We are concluding the data collection phase of a multi-country study that aims at documenting how research ethics committees (RECs) can be strengthened so that they can do a better job at filtering the CT designed by industry. We have used three instruments: in-depth interviews (about 100); focus groups (about 10), and a self-evaluation tool. The self-evaluation tool has not worked as well as we anticipated. The focus groups and the in-depth interviews have yielded very rich data. The conversations that we have had with the leaders in the different countries has in itself had an impact. The countries involved are: Argentina, Brazil, Colombia, Mexico, Peru, Panama, Dominican Republic, Costa Rica and El Salvador.

(more to come)

Members of ISDB posing with Gaspard Bonhomme, mascot of La Revue Prescrire (Photo by Jörg Schaaber)

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