International Society of Drug Bulletins

Newsletter

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ISDB General Assembly: preliminary announcement

Input from members needed!

The ISDB 2015 General Assembly will be held from 27–30 June 2015 in Pamplona, Spain.

At the meeting in Paris in July 2014, members of the Committee agreed on a list of criteria for topics that should or could be covered at the 2015 General Assembly. This list is summarised in the report of the Committee meeting, see p. 4.

In line with those criteria a suggested program was developed and this is published on pp. 2–3. There were also some suggestions made regarding possible speakers but, given that these people have not yet been approached, their names are not included in the draft program.

Before any more work on the program is done, the Committee would very much like some input from all members of ISDB.

Specifically, we would be very grateful if you could let us know:

- your comments on the suggested program, including topics, sessions, workshops;
- if there are other topics that should be covered;
- which of the proposed workshops you find of most interest;
- of any ideas you might have regarding possible speakers;
- whether or not you like the idea of a Members' Forum for members to give brief presentations on any new initiatives;
- whether or not you would be interested in attending a workshop on GRADE (in English or Spanish).

Please send any comments or suggestions you might have to Juan Erviti, ISDB Secretary, juan.erviti.lopez@cfnavarra.es.

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ISDB needs you

Join the Committee … become involved

Jörg Schaaber, ISDB President

The next ISDB General Assembly is closer than you think. It is only a little more than 6 months until we meet in Pamplona, Spain. This will not only be an opportunity to see colleagues and friends from all parts of the globe in beautiful surroundings, but also a unique chance to become actively involved in supporting and influencing the activities of the Society for the next three years.

The Committee needs strong representation – it is the lifeblood of the Society and it gives ISDB a voice in the world. The Committee's main work is to liaise with the membership to determine ISDB's agreed position on current issues and then to articulate this and make ISDB heard – whether it is advocating new rules for clinical trials in the European Union, or commenting on World Health Organization policy. Assessing new members, planning training workshops and a number of other tasks make being a Committee member interesting … and it is not too much of a burden. Each year the Committee has just one face-to-face meeting (for which travel support can be granted), two or three phone conferences and exchanges by e-mail.

Regional representation is an important factor as is diversity of competencies. So don't be shy and please consider being a candidate for election to the Committee.

If you are interested do write to me at president@isdbweb.org. Of course you can still apply at the meeting, but the earlier you think about it the better.

ISDB will need a new President

After the election in Pamplona the new Committee will meet to decide who will be the office bearers. The job of being President will definitely be available as I have already served two terms (6 years) as President. This is not only the maximum period allowed by the ISDB Constitution but it is also, I think, time for a change.

Footnote

The Constitution states that:

No person shall be appointed or reappointed to the Committee unless he/she:

(i) is recommended by the Committee; or

(ii) is willing to be appointed and has been nominated by at least two members of the Society.

General Assembly: draft program

Friday 26 June 2015

Arrival of Committee members

Saturday 27 June 2015

Day:	**Committee meeting**
Evening:	**Dinner and social activity for all participants** Welcoming addresses: Juan Erviti (Host), Jörg Schaaber (President)

Sunday 28 June 2015

09:00 – 11:00	**Plenary session: Regulatory challenges** – EU adaptive licensing & US expedited programme – Conflicts of interest at institutional level (e.g. WHO, EMA, patient groups) ***Suggestions for speakers required***
11:00 – 11:30	**Coffee break**
11:30 – 13:00	**ISDB activities** Reports on ISDB activities over past 3 years from President, Treasurer, Secretary, Coordinators of Working Groups
13:00 – 15:30	**Lunch and free exchanges**
15:30 – 17:00	**Workshops: Practice-oriented** – Editing a list of 'Do-not-use drugs' (Public Citizen, USA; Prescrire, France; arznei-telegramm, Germany; GeBu, The Netherlands)? – Making podcasts (Boletin de Información Terapéutica de Navarra, Spain; Therapeutics Initiative, Canada) – Using social media (Drug & Therapeutics Bulletin, UK)
17:00 – 17:30	**Coffee break**
17:30 – 19:00	**Workshops: Practice-oriented (repeat of early afternoon workshops)** – Editing a list of 'Do-not-use drugs' (Public Citizen, USA; Prescrire, France; arznei-telegramm, Germany; GeBu, The Netherlands)? – Making podcasts (Boletin de Información Terapéutica de Navarra, Spain; Therapeutics Initiative, Canada) – Using social media (Drug & Therapeutics Bulletin, UK)
19:00	**Photograph of all participants**
19.15	**Free evening**

Monday 29 June 2015

09:00 – 09:30	**Highlights from previous day** Reports from workshop rapporteurs
09:30 – 11:30	**Plenary session, Part A** Trade agreements and intellectual property rights: What are the implications for clinical data? ***Suggestions for speakers required*** **Plenary session, Part B** Introduction to Restoring Invisible and Abandoned Trials (RIAT) project & access to unredacted clinical study reports ***Suggestions for speakers required***
11:30 – 12: 00	**Coffee break**
12:00 – 13:30	**Workshops: Political** – How to obtain clinical data from regulatory agencies and what to do with it – Campaigning against unhealthy trade agreements
13:30 – 15:00	**Lunch**

General Assembly: draft program (continued)

15:00 – 16:30 **Workshops: Sharing experiences**

– Experiences in educating children about medicines (Natalia Cebotarenco, Moldova; Isidro Sia, Philippines; Benoit Marchand, Nicaragua)

– Sustainability: Continuing medical education as a source of income (Therapeutics Initiative?)

– Sustainability: How to develop a subscription-based bulletin (Prescrire, arznei-telegramm, Public Citizen)

– Evaluating a bulletin (Therapeutic Guidelines, Boletin de Información Terapéutica de Navarra, Therapeutics Initiative)

16:30 – 17:00 **Coffee break**

17:00 – 17:30 **Vote on proposed change* to ISDB Constitution**

(*refer to the report of the discussion regarding this issue by the Committee on p. 4 of this newsletter. Further clarification will be published in the next newsletter).

17:30 –18:30 **ISDB Committee elections**

19:00 **Meeting of newly elected ISDB Committee**

Decide on priorities for the next term

Free evening for others

Tuesday 30 June 2015

09:00 – 09:30 **Highlights from previous day**

09:30 – 11:00 **Plenary session: Pricing and reimbursement / RxISK**

Suggestions for speakers required

11:00 – 11:30 **Coffee break**

11:30 – 12:30 **ISDB Committee priorities**

Input from all General Assembly participants

12:30 – 13:30: **Members forum**

Short (2-minute) presentations and/or posters from members on their bulletins, on-going campaigns, new initiatives etc. (proposals/abstracts to be sent in advance to Juan Erviti, ISDB Secretary)

13:30 – 15:30 **Lunch**

15:30 – 17:00 **Workshops: Sharing experiences (repeat of previous afternoon's workshops)**

– Experiences in educating children about medicines (Natalia Cebotarenco, Moldova; Isidro Sia, Philippines; Benoit Marchand, Nicaragua)

– Sustainability: Continuing medical education as a source of income (Therapeutics Initiative?)

– Sustainability: How to develop a subscription-based bulletin (Prescrire, arznei-telegramm, Public Citizen)

– Evaluating a bulletin (Therapeutic Guidelines, Boletin de Información Terapéutica de Navarra, Therapeutics Initiative).

17:00 – 17:30 **Coffee break**

17:30 – 19:00 **Plenary session (open lecture): Overdiagnosis and overtreatment (disease-mongering)**

Facilitator: new President

Suggestions for speakers required

19:00 **Closing remarks from new President**

21:00 – 23:00 **Dinner and social activity**

Wednesday 1 July 2015

09:30 – 13:30 **GRADE Training**

The Grading of Recommendations Assessment, Development and Evaluation (method set up and used by the Cochrane Collaboration). A sensible and transparent approach to grading quality of evidence and strength of recommendations.

Two concurrent workshops (one in English, one in Spanish). Therapeutics Initiative will collaborate with Boletin de Información Terapéutica de Navarra to prepare the training session which will be offered in English (Therapeutics Initiative) and also in Spanish (Boletin de Información Terapéutica de Navarra).

Report: ISDB Committee meeting, July 2014

A meeting of the ISDB Committee took place in Paris on 10–11 July, 2014. People who attended the meeting were:

Jörg Schaaber
PharmaBrief, Germany (*Chair*)

Juan Erviti
Boletin de Información Terapéutica de Navarra, Spain (*Secretary*)

Natalia Cebotarenco
Medex, Moldova

John Dowden
Australian Prescriber, Australia

Mary Hemming
Therapeutic Guidelines, Australia

Ciprian Jauca
Therapeutics Initiative, Canada

Benoit Marchand
Boletin AIS-COME, Nicaragua

Zahed Masud
Drug and Health Bulletin, Bangladesh

Isidro Sia
RDU Update, Philippines

Florence Vandevelde
Prescrire, France

Maria Font (unable to attend the meeting)
Infofarma, Italy

Teresa Alves (by invitation)

Nuria Homedes (by invitation)

General Assembly 2015

It was agreed that the dates for the General Assembly will be from Saturday 27 June 2015 to Tuesday 30 June 2015. The Committee members will meet on Friday 26 June and on July 1 there will be an optional training session on Cochrane methods for all General Assembly participants.

Discussion took place about the program for the General Assembly and it was agreed that topics for the meeting should be chosen according to the following criteria:

- likely impact (for Bulletins as well as for society),
- international relevance,
- usefulness,
- awareness-raising topics,
- developing practical skills,
- specificity,
- cost of speakers.

ISDB website

Ciprian Jauca reported that he had obtained an estimate for the cost of a new website for ISDB. It was noted that the project could be divided into various stages so only a portion of the full amount would be required to start the project.

Ciprian Jauca undertook to forward a project proposal to the Committee members. This issue will be further discussed by the Committee in a phone conference in the forthcoming months.

It was noted that the members' forum section of the current ISDB website does not work well and is used very infrequently. It was proposed that, as an interim measure, another forum should be established in its place until the new website is ready.

Newsletter

Mary Hemming presented a report on the newsletter including a summary of the articles that have been published over the past two years.

It was noted that there is not enough content being submitted to allow three issues per year. It was agreed that two issues per year would be sufficient.

It was agreed that the next issue would contain information about the 2015 General Assembly including a draft program and members will be invited to send their comments and suggestions.

Working groups

Reports on the activities of the ISDB working groups were given by Teresa Alves (Advocacy), Nuria Homedes (Clinical Trials) and Natalia Cebotarenco (Educational Information for Health Workers and Consumers).

The reports from these three groups are published separately in this newsletter.

Conflict of interest policy

The policy of ISDB on conflict of interest (CoI) was discussed. All members agreed that the editorial team of a bulletin must be free from any CoI with pharmaceutical and healthcare related companies as stated in the ISDB constitution (article 2a). Some ISDB bulletins are able to use in-house editors to prepare all their articles and therefore can be considered to be completely free from CoI. Other bulletins commission external authors to contribute to articles and, in this case, CoI may arise when external authors have CoI. The majority of Committee members agreed that external authors should be free from CoI as well. A question was raised about institutions that publish bulletins and also undertake research sponsored by pharmaceutical companies, but the issue was not discussed in depth.

There was discussion about whether the General Assembly should vote on an amendment to the constitution to state that to be granted full membership bulletins should not use external authors with potential CoI. Concern was expressed that a vote could split ISDB.

The Committee voted in favour (seven for, three against) of holding a vote at the General Assembly.

Therefore the Committee will put a resolution to the 2015 General Assembly proposing an amendment to the ISDB constitutions in the following terms:

- External authors should be free from CoI for the bulletin to be granted full membership.
- There will be a three-year period for full members to adjust to this new situation.
- The three-year adjustment period will not apply to new members.

When the new regulations come into effect, bulletins that have external authors with CoI or directly undertake sponsored research will be granted associate membership. These bulletins will be allowed to use an 'ISDB Associate Member' logo.

In the coming months the Committee will discuss ways to reinforce and promote an active role of associate members within the ISDB.

In addition, the Committee will explore how to expand the network and liaise more closely with other organisations that also produce information on drugs and therapeutics (blogs and similar platforms) but not necessarily bulletins as such, and enquire about their interest in becoming associate members.

Working group report: Clinical trials

Nuria Homedes, Coordinator

English version published

The publishing house, Springer, in The Netherlands published the English version of our book, *Clinical Trials in Latin America: Where Ethics and Business Clash*, N Homedes and A Ugalde (Editors), 2014.

Clinical trial registries

The Journal of Medical Ethics has accepted an article we wrote on the use of inappropriate codes in the USA Federal Clinical Trial Registry by Bayer, and the lack of external support for research ethics committees in Latin America. The title of the article is *The evaluation of complex clinical trial protocols: resources available to research ethics committees and the use of clinical trial registries: A case study*. Even though we know the article has been accepted, we do not know when it will be published.

We have collected information on the different clinical trial registries in Latin America to assess whether or not they duplicate the information available in the global registries (WHO, USA, Europe) and to discuss how they could be adapted to the needs of Latin America. However, the Pan American Health Organization does not seem to be advocating national registries anymore so we might abandon this initiative.

Informed consent

We conducted some in-depth interviews with clinical trial participants in Peru. The project was part of a masters thesis and we aim to publish the work. The main findings were:

- participants know they are part of a project but they have not been told that it is an experiment;
- most people agree to participate because they think they will receive better treatment;
- not all participants know that they should report all adverse events, and that they should not self-medicate or use alternative medicine.

The regulatory agency in Peru has included interviews with clinical trial participants in the protocol for clinical trial inspections.

Ethics committees

We are starting an ambitious study to ascertain how ethics committees can be strengthened in Latin America. We are collecting information (regulatory framework and existing publications) from the following countries: Argentina, Brazil, Colombia, Chile, El Salvador, Mexico, Panama, Paraguay, Uruguay and Spain. We intend to conduct in-depth interviews with ex-members of ethics committees and with regulatory agencies in a subsample of these countries in 2015. The methodology for the second part of the study will be discussed at a regional meeting in late 2014.

New FDA approvals

We have collected information on new molecular entities approved by the FDA in 2011 and 2012. Using FDA information and through contacts with clinical trial sponsors we have identified the developing countries where the pivotal clinical trials were conducted. We are now collecting information on the prices of those products in the countries where they were tested. We are discovering that industry has not registered these products in countries where there is no lucrative market.

Working group report: Advocacy

Teresa Alves, Coordinator

The ISDB Advocacy Working Group meets monthly by telephone to discuss ongoing developments in pharmaceutical policy. There have been several developments in Europe that the group has followed closely. This report covers activities for the period January–June 2014

European regulation of clinical trials

In July 2012, the European Commission released a new draft European Regulation on clinical trials. The aim of the proposals was to deregulate research conducted on humans. All reference to ethics committees was removed and certain measures would have left Member States incapable of protecting participants in clinical trials conducted in their country. Due to the mobilisation of many organisations representing civil society (including ISDB) several measures to protect trial participants were reinstated. The need for independent, critical analyses of the results of clinical trials also emerged in the parliamentary debate.

The new Clinical Trials Regulation (Regulation (EU) No 536/2014) was adopted in May 2014 by a huge majority. This was the result of intense efforts by the Parliament, Council and civil society. The regulation will be implemented by mid-2016.

Centralised applications

The new regulation enables clinical trial sponsors to submit a single request, via a centralised portal, for all the countries in which they would like to conduct their clinical trial. The request undergoes joint 'scientific' review by the Member States concerned, coordinated by a 'reporting Member State'. In parallel, each Member State must conduct an 'ethical' review. In practice, this ethical review is limited to checking how informed consent is obtained. The trial is automatically authorised if the authorities do not respond within the stated deadlines (tacit authorisation). If a national ethics committee issues a negative opinion, the trial cannot be conducted in that country.

Greater transparency

The new regulation creates greater transparency of clinical trial data and results. It establishes that Clinical Study Reports (CSRs) 'should not be considered commercially confidential once a marketing authorisation has been granted, the decision-making process on the application for a marketing authorisation has been completed, or an application for marketing authorisation has been withdrawn'. This is in accordance with the policy on access to documents held by the European Medicines Agency (EMA), which has been in effect since 2010. Additionally, CSRs must be made publicly accessible within 30 days of the marketing authorisation being granted and penalties will apply if this deadline is not met.

Limitations

The policy-makers did not seize the opportunity to demand that the evaluation of new drugs must include trials comparing them with standard treatments. Worse still, this new regulation considers certain clinical trials in which a drug is used outside its authorised indications (off-label use) as 'low-intervention' trials which, as such, are subject to less stringent regulation.

This new European Clinical Trials Regulation (Regulation (EU) No 536/2014) could still constitute an unprecedented advance in terms of transparency, unparalleled in the world. However, will the regulation, once implemented, bring about the transparency that is needed? Only time will tell.

For a detailed overview, please read: http://english.prescrire.org/en/79/207/46302/3315/3303/SubReportDetails.aspx

Development of a new policy on access to clinical data

ISDB has been monitoring the development of the EMA's policy on publication and access to clinical trial data since November 2002. We submitted a joint response to a public consultation in September 2013 (read online:http://english.prescrire.org/Docu/DOCSEUROPE/20130927JointSubmissionEMAtransparency.pdf); and participated in working groups on the new policy.

We welcomed the EMA's move to become more transparent and provide access to important clinical data on the efficacy and safety of medicines. However, in May 2014, the EMA shared documents during a stakeholder consultation that revealed a watering down of its 2013 draft policy on access to clinical data. There is now a risk of systematic censorship by pharmaceutical companies, strict confidentiality requirements and wider restrictions on the use of the data, including viewing the content of clinical study reports on screen-only, with no possibility to download or save the documents.

This backwards step occurs in the context of negotiations on the Transatlantic Trade and Investment Partnership (TTIP). This is a bilateral trade agreement between the European Union and the USA, where strong pressure is being exerted to uphold commercial interests.

ISDB issued a joint press release with the Association International de la Mutualité (AIM), the Medicines in Europe Forum and Nordic Cochrane Centre about the dangers of this new version of the policy to raise awareness among the EMA Management Board, the media, the European Commission, Members of the European Parliament, policy-makers and drug regulatory agencies. Following a public outcry, the EMA announced on 12 June that the management board had asked for the removal of the screen-only restrictions, granting the 'possibility to download, save and print the trial data for academic and non-commercial research purposes'.

While some might herald these changes as a victory, ISDB has advised caution and continues to have serious concerns about the proposed EMA's 'redaction principles' and 'terms of use', which underlie this new policy. Several restrictive measures and legal loopholes were left unaddressed. We issued a second joint press release in response to EMA's announcement (available at http://english.prescrire.org/Docu/DOCSEUROPE/20140624_EMAnewPolicyAccessClinicalData.pdf).

The adoption of the policy has been postponed until the meeting of the EMA Management Board in October 2014. The Advocacy Working Group will keep on monitoring this issue.

Response to a consultation on disclosure of data

In April 2014, ISDB, HAI Europe, Medicines in Europe Forum and the Transatlantic Consumer Dialogue made a joint response to a consultation by the US Institute of Medicine about the disclosure of clinical trial data. We have encouraged the active implementation of a data sharing policy that ensures full public access to clinical data in the USA, in alignment with the new European requirements. The full response is available at: http://english.prescrire.org/Docu/DOCSEUROPE/20140404_ConsultationTransparencyIoM.pdf

EU regulation on medical devices

The European Commission's proposal on medical devices was published in July 2012 and amply discussed at the European Parliament. However, the dossier was not finalised by the end of the last legislature (Spring 2014). This legislative proposal is currently on stand-by. The discussions between the European Council, Commission and Parliament were scheduled to begin after September 2014.

Trouble with TTIP

The Transatlantic Trade and Investment Partnership (TTIP) is an agreement currently being negotiated between the European Union and the USA.

A report released on 24 March 2014 by a coalition of civil society organisations, including ISDB, has shown that the pharmaceutical industry's wish list for the TTIP is detrimental for public health. Among other problems, greater protection for pharmaceutical companies is likely to limit price competition with generic products.

The full report available at: http://english.prescrire.org/Docu/DOCSEUROPE/20140324CivilSocietyResponseBigPharmaWishList_final.pdf

Trade secrets

On 28 November 2013, the European Commission published a proposal for a directive on trade secrets. This includes a very broad definition of trade secrets and several worrying provisions that encourage litigation. The confidentiality of trade secrets would be maintained during and after legal proceedings, and other measures establish dissuasive sanctions. This legislative proposal was well-received by the trade association of the European pharmaceutical industry (EFPIA).

In view of these developments, ISDB alerted the Members of the European Parliament to remain very vigilant during the forthcoming discussions on this directive, and to make sure that clinical data on pharmaceutical products and medical devices remain outside the scope of this directive.

If you would like more information about the Advocacy Working Group, please contact Teresa Alves at talves@prescrire.org.

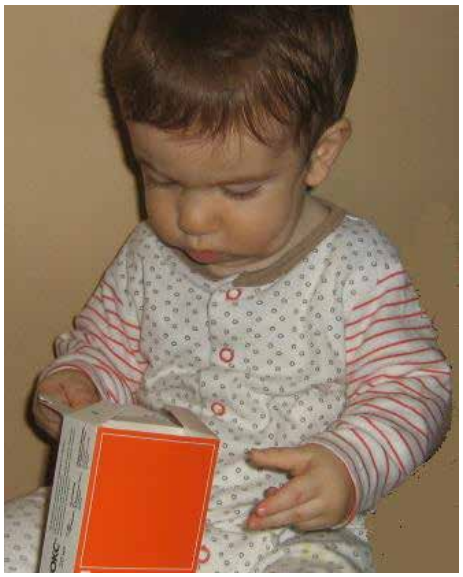
Working group report: Educational information

Natalia Cebotarenco, (Coordinator), Isidro Sia (Philippines), Benoit Marchand (Nicaragua) and Zahed Masud (Bangladesh)

Advocacy campaign: Candy for children should not look like medicine

This group has members from both the developed and developing world and we undertake activities in many countries including Austria, Bangladesh, Burkina Faso, Canada, Colombia, Costa Rica, Croatia, Cuba, India, Moldova, Nepal, New Zealand, Nicaragua, Philippines and USA. Public health problems vary from country to country so we looked for a theme for an advocacy campaign that is common to all countries and which focused on children because they are the future generation. The theme we chose was Candy or Pills? Candy for children should not look like medicine.

Children are curious by nature, so it stands to reason that they are also curious about medicines. Many pills are shiny, round and unmarked so they look, and even taste like, candy. Children are getting poisoned accidentally because some candy and medicine are hard to tell apart even for adults.



Curious Sasha!

It's important to encourage children to explore and discover new things, but when it comes to medicines the overriding principle should be to make sure that children are not at risk. Unfortunately, parents and grandparents often persuade children to take their medicine by telling children that pills are just candy. This message is dangerous as it not only gives children incorrect information but it leads them to believe that pills are safe. Unless children are otherwise informed it is likely that if children find discarded pills they might eat them thinking they are candy, not knowing of the danger.

Participants from Moldova, Ukraine, Armenia, Kazakhstan at a workshop to develop a collaboration to ensure the safety of medicines for the younger generation
October 2014

How big is the problem?

The US organisation Safe Kids published a report in March 2014 entitled 'Keeping Families Safe Around Medicine'[1]. According to the report, every minute of every day, a poison control centre answers a call about a young child getting into medicine or getting too much medicine. In 2012, there were almost 64,000 emergency department visits that involved a child exposed to medicine. Every one of these emergency department visits involved a scared child and a worried family, and could have been prevented. On top of that, an estimated $34.4 million is spent every year on medical costs for trips to the emergency department as a result of medicine exposures in young children, twice what the federal government spends annually on poison control centres.

Pilot study in Moldova

A pilot study was designed by members of the Coalition for Rational and Safe Use of Medicines (CoRSUM) in Moldova. The goal of the study was to determine if children, their carers and community pharmacists can differentiate between pills and candy. The study was conducted in two schools in Chisinau in September 2014. It involved 45 students who were aged 10 years, and their grandparents. The children, the grandparents and the group of 22 pharmacists were all tested separately. A presentation of 30 slides was prepared. On each slide were two pictures of items similar in shape, colour and size. Grandparents and children were asked to identify which item was a pill and which was candy. The results showed that only 2–3 percent of children and 7–9 percent of grandparents were able to identify the items correctly. Only 40–45 percent of pharmacists gave the right answers.

From this preliminary study it was concluded that, practically speaking, neither children nor their grandparents are able to distinguish between pills and candy.

What can be done?

The problem of children being poisoned with pills is a growing issue around the world. One of the biggest reasons for this is that candy manufacturers make candy in the shape of pills. This practice must be recognised as being very dangerous for children and should be stopped by means of worldwide advocacy campaign. ISDB should play a leading role in such a campaign.

Members of the ISDB Educational Information Working Group will continue its work to investigate the problem in their countries using the methodology of the pilot study. We will continue to collect examples of the similarity between candy and pills, and to develop educational materials such as video and booklets. The advocacy materials will be presented at a workshop at the 2015 General Assembly in Pamplona, Spain.

1. http://www.safekids.org/med_report_2014

Conversations with bulletins

The Drug and Health Bulletin of Bangladesh (Ashud–O–Shasthy)

Dr Zahed M Masud, Chief Editor

Standing (left to right) Saiful Islam, Mina Akhter (Documentation Officer), Dr Zahed M Masud
Sitting (left to right) Dr Fauzia Begum, Dr Khurshid Jahan (Member of Editorial Board)

Why was your bulletin started?

There is little independent drug information in Bangladesh. Patients do not have access to essential information about drugs. This means patients are more likely to suffer adverse drug reactions, and it leads to an increased incidence of low compliance, failure of therapy and emergence of antibiotic resistance.

The main source of drug information available to most physicians after they graduate from medical college, comes from the pharmaceutical industry. The lack of reliable information for physicians is a serious problem, especially with the increasing number of drugs coming on to the market as a result of liberalisation in Bangladesh.

Policy makers and regulatory authority do not have access to unbiased and independent information so their decisions are based on information provided by the drug manufacturers. Consequently many ineffective and expensive drugs are entering the market.

To address these problems, a group of people from different disciplines volunteered their time and effort and made a commitment to publish independent information about drugs and health regularly every three months.

The aim of the bulletin is:

- To educate patients about drug use and to promote awareness of consumers' rights.
- To provide unbiased and independent information to policy makers and the regulatory authority to make proper decision in favour of the people.
- To provide reliable information to pharmaceutical companies to encourage them to produce useful, affordable, safe and high quality essential drugs in line with the needs of the country.

How long has your bulletin been going, how often do you publish it and who receives it?

The Drug and Health Bulletin was first published in November, 1999. It is a quarterly bulletin and is distributed to prescribers, general practitioners, medical colleges, institutions for students, relevant government ministries and policy making directorates, and also to various international organisations.

What staff and resources do you have to produce the bulletin?

All members of the editorial team are volunteers who give their time and provide funding to support the publication and distribution of the bulletin, and to organise various events.

The group is comprised of doctors, medical students, and people from different media.

Do you liaise with other like-minded organisations in your area?

There are not many like-minded organisations in Bangladesh, especially in the area of rational drug use. There is a peoples' health movement (Health for All) and also the Consumers Association of Bangladesh, but health is only a small part of their focus.

What kind of issues do you cover in your bulletin?

Many articles published in the bulletin cover policy and advocacy issues: to support a drug policy that benefits people; to advocate better policies to promote the rational drug use; to withdraw harmful and ineffective drugs; to raise awareness about the quality of drug manufacturing and price issues; to draw attention to aggressive marketing practices by pharmaceutical companies; to promote continuing education for prescribers; and to advocate the rights of people to achieve better health outcomes.

Articles are also published covering research and reports on drugs, campaigns for better drugs, news about work done internationally by drug and health activist groups.

What are your main challenges for the future?

The big challenge is the threat posed by the pharmaceutical industry, which is supported by powerful people in society and sometimes even by the politicians. There is little support in the community, or from organisations, or even from government, for independent information and the rational use of drugs. Finding funds from acceptable donors to support the publication of the bulletin is also a big challenge.

Therapeutics Letter, Canada

Dr James M Wright, Editor-in-Chief and Ciprian Jauca, Managing Editor

Why was your bulletin started?

The Therapeutics Initiative was started in 1994 when a proposal was submitted to the British Columbia Ministry of Health to set up a program to provide evidence-based drug therapy information to clinicians. Dr Casey van Breemen, then newly appointed Head of the University of British Columbia Department of Pharmacology & Therapeutics and Dr James M Wright, Clinical Pharmacologist, led this proposal. PharmaCare, the division of the Ministry of Health responsible for covering the cost of prescription drugs in British Columbia, was experiencing the negative effects of the exponential increase in drug costs at the time and was therefore receptive and decided to fund the proposal.

How long has your bulletin been going, how often do you publish it and who receives it?

In October 2014, we celebrated 20 years since the publication of the first issue of the Therapeutics Letter, a bi-monthly drug bulletin published by the Therapeutics Initiative (TI). Over 90 issues have been published since 1994. Approximately 15,000 paper copies are mailed to the prescribing and dispensing physicians and pharmacists in British Columbia, medical students, residents and various allied healthcare professionals. An electronic copy is posted on the TI website www.ti.ubc.ca and is freely available to anyone with access to the internet. Currently the TI web site receives over 25,000 visits per month.

What staff and resources do you have to produce the bulletin?

The Therapeutics Initiative (TI) is funded by a grant to the University of British Columbia. The first decade of TI's existence was characterized by steady growth. The initial TI grant was for $525,000 per year for 5 years. In 1999, after the successful completion of the first 5 years, the grant for the TI was increased to $700,000 per year and in 2004 it was further increased to $1,000,000 per year, while additional funding was also made available for special projects. From 2008 onwards, political interference, most likely due to lobbying by pharmaceutical companies, eroded the government's support of the TI and led to a decrease in funding in April 2012 to $550,000 per year, and in October 2012 the TI funding was suspended. As a result of a successful public awareness campaign vigorously pursued by the TI, the funding at $550,000 per year was reinstated in January of 2014. However, due to the suspension from October 2012 to January 2014, only one Therapeutics Letter (issue #88) was published between September 2012 and March 2014, with a different funding source.

The Therapeutics Letter is produced by a team consisting of an Editor-in-Chief, two to three sub-editors, a copy/managing editor, and a graphics designer/publisher. The evidence-based information in the Therapeutics Letter is produced by a team of 5–10 researchers in the TI Drug Assessment Working Group, often complemented by analyses of drug utilization produced by a team of 5–10 researchers in the TI Pharmaco-Epidemiology Working Group.

Do you liaise with other like-minded organizations in your area?

We liaise closely and share some of the same staff with the Cochrane Hypertension Group. We collaborate with the International Cochrane Collaboration and particularly with Cochrane Canada. We maintain collaborative links with many ISDB bulletins around the world.

What kind of issues do you cover in your bulletin?

We focus particularly on issues related to drugs commonly prescribed in the community. Thus our Letters are of most interest to family practice and general physicians plus community pharmacists.

What are your main challenges for the future?

Our experience has taught us that even democratically elected governments are vulnerable to lobbying by powerful vested interest groups. Our main challenge is to train and retain individuals who are skilled in systematic review in order to continue to produce high quality information for future Therapeutics Letters. At the present time our funding is insufficient to support these people and we are constantly looking for other sources of funding to maintain a critical mass with the required expertise.

What are the side benefits that have come from publishing your bulletin?

The pattern of drug utilization in British Columbia is markedly different from the rest of Canada, with drug expenditure in British Columbia estimated to be $1000 million per year less than the national average, while both life expectancy and overall health indicators for British Columbians are superior to the rest of Canada.

When the Therapeutics Letter started 20 years ago we did not expect to have much impact outside of the province of British Columbia. An unexpected side benefit is that for many of our publications the impact outside British Columbia has been even greater than locally. This has occurred because of the wide reach of the internet and positive press coverage. We have also had impact on the Spanish-speaking people of the world through ISDB-facilitated liaisons with Spanish colleagues leading to translation of the Therapeutics Letter into Spanish. Another side benefit is that we discovered unexpectedly that some of our Therapeutics Letters are being cited in the scientific literature.

Pharmacovigilance still neglects patients

Andrew Herxheimer

Pharmacovigilance work should enable us to ensure that the benefits of treatment outweigh the harms it may cause. The most difficult part of it is to weigh the benefits against the harms for the individual patient, not only for the population as a whole.

Doctors should be able to explain to a patient why a particular medicine (or other treatment) is worth using, and to help them do that we need to know as much about the possible harms as about the likely benefits. But we know vastly more about the benefits than the harms, for several reasons:

1. We look for particular specified benefits, but we must watch for any kind of harm, not only those that cause most anxiety.
2. In the treatment of many illnesses, benefits begin long before harms are noticed.
3. Far more resources are used for work on benefits than for work on harms, in academia, in industry, in drug regulation and in other public institutions. For example in 2010 the Licensing division of the UK regulatory agency (the MHRA) had 270 scientific staff, its Vigilance division 144.

So how can we fairly weigh a treatment's benefits against its possible harms?

Getting reports on suspected harms

Because we don't know what harms to look for, we must all, whether doctors, nurses, pharmacists or consumers/patients, be alert for signs of possible harm. Regulators in many countries now accept reports of suspected adverse drug reactions (ADRs) directly from consumers, but they receive few – most people are still unaware of the scheme. Regulators and health professionals have not yet learnt how best to encourage such reporting, nor how to use the reports effectively.

Doctors and nurses are not accustomed to observing, recording and investigating adverse events that might be ADRs; patients and carers have not learnt to do it.

One potentially important though minor source of data on suspected harms has so far not been used: legal claims against pharmaceutical companies for drug injury. Only claims heard in court are published, but many are settled out of court and details remain secret – so we don't know how many such cases occur. Secrecy for settled cases disadvantages other drug users and should be outlawed.[1]

In a drug regulatory agency assessors classify and code the ADR reports according to a dictionary of terms (Medical Dictionary for Drug Regulatory Activities MedDRA; www.meddra.org), and look for evidence that the medicine was a cause. MedDRA is updated twice a year and helps regulators and the companies they regulate, but not doctors, patients or academic researchers.[2] The updating disregards events that are not medically recognised. A striking example were 'head shocks' which patients commonly report during withdrawal of paroxetine and other SSRI antidepressants. This emerged when we compared reports submitted by patients with reports from professionals: the MHRA coded 'head shocks' as 'paraesthesia', the technical term for 'abnormal sensation' used not only for a shock or for the head.[3]

Often causality remains uncertain, partly because reports lack relevant details, and that makes it difficult to act on the report. Detailed descriptions can tell us much that we don't know and need to know, but they mostly don't appear in the coded reports. We should all encourage those who report adverse events to ask the affected persons to describe what they experienced and how it has affected their life.

Assessors must also decide whether the harm was 'serious' or 'non-serious', and what, if anything, should be done about it. Although regulators define a 'serious' event as an 'important medical event', such as death or admission to hospital, to everyone else it means 'serious for that person'. But seriousness is subjective and is therefore most reliably and meaningfully determined by the person affected or someone personally close – no-one else, however professional, can properly assess it. Those who have experienced harm should be heard.

Adverse events likely to be misclassified as non-serious are those that are mainly subjective and only indirectly verifiable, if at all. Such events may cry out for follow up. Examples are pain, sexual difficulty, or misbehaviour leading to divorce, job loss, or crime.

Follow-up, access to reports, and research

Views of the seriousness of a particular event often change with time, so may need to be followed up with the reporter, whether professional or patient – but follow-up is haphazard. The reporter, whether a professional or a member of the public, usually gets no feedback from the agency, only a formal acknowledgement. Cases are rarely followed up. We need conventions on follow up based on the importance of particular harmful effects and what is known about their time course.

The detailed reports in the agency's database are 'confidential' and not accessible to outsiders; access for research requires specific permission. Confidentiality is invoked to protect the identity of patients and reporters, but it also obscures decision processes in the agency.

Research is not an acknowledged function of regulatory agencies though they have mountains of data that need analysis in the public interest. That would best be done separately through national research organisations such as the US National Institutes of Health, or the UK National Institute of Health Research.

It is hard to resist the conclusion that reports of suspected harms from consumers should be managed at arm's length from drug regulatory agencies, in close collaboration with them, but with separate funding and staff.[4]

Warnings about possible harms

When a medicine is licensed, the licence holder submits the proposed texts about it to be given (a) to health professionals and (b) to patients. The regulator and licence holder, advised by lawyers, privately negotiate the final texts of the SPC (Summary of Product Characteristics) and the PIL (Patient Information Leaflet). These are legal documents which must be updated and give the date of preparation. Regulators assume that they give everyone access to appropriate and correct information, and that people are responsible for acting on it.

PILs list possible harms and side-effects without describing or explaining them, so

that a person cannot properly consider them before deciding whether to use the medicine. Some just seem to be a legal defence for the licence holder, saying 'you were warned'.

What is known about possible harms and precautions at the time of first licensing of a product comes mainly from studies in healthy volunteers and patients in clinical trials. The populations studied, and the methods of study and ascertainment in these groups differ greatly from the much bigger and more diverse populations exposed when the drug is marketed, which are the main source for spontaneous reporting systems. How regulators combine the adverse effect data from these two very different sources is unclear. The tabulations in the Yellow Card database seem to include only the spontaneous reports from use in practice.

Most recently the public information about adverse drug reactions has been justly criticised as excessive, inconsistent and confusing.[5]

Probably few health professionals read and assimilate what is in the SmPCs for the drugs they prescribe, dispense or administer. These are boring and unattractive. The final draft texts of SmPCs should be pilot-tested on groups of health professionals, but this does not happen. Likewise we don't know how far patients and their carers understand and use the PILs. Many don't even read them.[6, 7] How should we identify users who cannot understand them, and how can we help them? Since 2005 the text of PILs must be tested 'for readability' on volunteers on behalf of the licence holder and submitted to the regulator, but the tests are inadequate.

A doctor, pharmacist or nurse with patients who do not understand their medicine may try to explain it and teach the patient about it. As Michael Balint reminded us, 'doctor' originally meant 'teacher', but now few teach; none are encouraged or helped to do so. This largely prevents concordance[8] and shared decision making.[9]

Information is not education

Choosing appropriate drug therapy, and using it effectively and safely, requires understanding of some basic general principles about medicines and their uses, and how to apply these principles in considering particular medications.

Few members of the general public are aware of these principles, which they need to think sensibly or coherently about drugs. They must depend on what they hear from prescribers or allied professionals, or what they read or hear from other sources, whose reliability they cannot judge. The huge gap between professionals and patients in understanding health and illness is the greatest barrier to 'shared decision making', which all patients who want it should be offered. However, discussions about this fundamental problem in health care talk about 'informing' patients and the public, and have not addressed the need to educate people and make them 'health literate'. People who cannot assimilate and process 'Information' cannot use it to their advantage. The structure and the brevity of consultations allow no systematic teaching of the underlying principles.

Principles which people have to grasp to understand drugs[10]

- Categories and names of drugs
- The different uses of drugs (preventive, supportive, symptomatic, curative, or diagnostic)
- How drugs reach the site of action
- How drugs produce their effects and the time course of drug actions
- Drug interactions
- How drug effects are demonstrated and investigated[11]
- Sources of information and their trustworthiness
- Treatment guidelines and recommendations

Applying the principles requires some knowledge of the disease or problem to be treated, and how and in what circumstances the drug can influence it. We must consider both positive and negative effects of the drug to weigh its estimated benefit against the possible or likely harms from it.

How can we get there?

We need to separate 'Official information' about medicines from public education. We must distinguish between information and education: people who don't understand the principles cannot properly use health information and are left out.

The simplest approach would be to integrate the principles with the information, that is, to make them an inseparable part of Patient Information Leaflets (PILs) and perhaps of Summaries of Product Characteristics (SPCs). That would facilitate fruitful discussions between patients and professionals, such as pharmacists, nurses and doctors. In 1995, the then new European Directive on the contents of PILs mentioned none of the principles nor supported the good conversations between patients and professionals that enable decisions to be shared.

In designing PILs it is high time to put the interests of patients and health professionals first. For instance, the mindless repetition of the brand name in PILs is mere promotion – obtrusive and absurd.

Separate programs to educate the public to understand and apply the principles require much more effort and resources, but we should consider what methods are worth trying for different target groups.

For schoolchildren, the principles could fit into biology or domestic science teaching, starting in secondary school or earlier. Their teachers would also need a teaching package. For adults, web-based learning seems the best option. Web-based programmes could be supported by the health system and professional bodies, through public libraries and local community services, and not least patients' organisations.

Specific groups for targeting could include young mothers, carers of chronically ill people, and retired people. The last would benefit disproportionately from better understanding of medicines, and have more time – they deserve special programmes.

Andrew Herxheimer photographed in Japan after giving a talk on pharmacovigilance

Although print and broadcast media also have important roles, frothy news appeal and editorial values often work against real understanding.

Conclusion

Pharmacovigilance has become a part of medicines regulation in collaboration with the pharma industry, but it has not adequately considered the personal interests and needs of patients and the public. No attempt has been made to bridge the gap between administrative handling and evaluation of ADRs and the possible devastating experiences of such harm by some patients.

After half a century it is time to restructure pharmacovigilance in the interests of patients and the public, and manage it through structures responsible for research, health services, and public education. Of course we will continue to need the industry and regulators, but they cannot be left to decide what best serves the public interest, nor to influence education of the public. I hope that countries will collaborate and compete to achieve this quickly.

Permission and encouragement is given to translate this article into other languages! We need the improvements everywhere and should not wait! (Andrew Herxheimer)

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Noticeboard

Committee member's award

The Royal College of Physicians of Edinburgh was formed in 1681 to improve the practice of medicine. It is still involved in setting the standards of practice and it influences health policies with the aim of improving patient safety and the quality of care.

Although the College is based in the United Kingdom, it can award Fellowships to overseas doctors who have made a significant contribution to medical practice.

Dr John Dowden, the Editor of *Australian Prescriber,* was recently nominated for one of these Fellowships for his contribution to drug education in Australia and internationally. He is seen here receiving his award from Professor Derek Bell, the President of the College, at the official ceremony in Edinburgh in June this year.