



Vol. 16, N°2, July 2002

NEWSLETTER

COLUMN

IMPORTANT

A date for your diary!

**GENERAL ASSEMBLY
19-21 SEPTEMBER, 2002
DUBROVNIK, CROATIA**

Fill in a registration form
via the ISDB website
www.isdbweb.org

—————
*Details of the agency in
charge
of accommodation*
—————

Gulliver - Dubrovnik

Contacts: Marina Tomic and
Zdenka Talijic

Telephone:
+385 20 313-300; 313-305

Fax: +385 20 419-129; 419-119

E-mail: gulliver@gulliver.hr
Website: www.gulliver.hr

Dubrovnik soon!

Time to meet together is coming. You'll find in this issue the detailed programme of our general assembly and workshops. The meeting will be all the more fruitful if all of us prepare for it in advance. We invite you to bring any material you would like to share with colleagues. There will be room for a poster exhibition, and enough tables to put copies of your bulletins on display.

The meeting is a good opportunity to bring any document sources you may have discovered in the last three years, and that you would like to show either because they are reliable and helpful, or simply too bad. Such sources can be produced in your country or internationally: guidelines, textbooks, websites, etc.

The most wicked direct-to-consumer ads are also welcome for the poster session, as well as funny stories.

Contents

COLUMN

Dubrovnik soon! p. 1

NEWS OF ISDB

ISDB General Assembly p. 2

Guidance for effective communication at the GA p. 3

ISDBweb.org p. 5

NEWS OF BULLETINS

Metamizole in Moldova p. 6-9

Arznei-telegramm and unfavourable data p. 10

Lundbeck plays foul in Sri Lanka p. 11

Lobbying campaign by ISDB Europe p. 12

The Eritrean list of drugs p. 12

La revue Prescrire on bupropion/amfebutamone p. 12

ISDB WORKSHOPS AND GENERAL ASSEMBLY

19–21 September 2002 - Dubrovnik, Croatia

THURSDAY 19th

- 9.00** Coffee ☕
- 9.30** Welcome from Bozidar Vrhovac
(**Chair for the morning session**)
and address by a representative of
the Croatian health authority
- 9.45** Reports from the executive committee, 1999–2002
- Chairman's report
- Treasurer's report
- General Secretary's report
- 10.15** Presentation of the new members of ISDB
- 11.00** Coffee break & poster exhibition ☕
- 11.15** Short presentations from the regions
- Africa: Georgette Sanou, to be confirmed
- Asia Pacific: (1) Hirokuni Beppu, (2) John Dowden,
to be confirmed
- Israel: Philip Sax, to be confirmed
- Central Asia: Gita Fernando
- Eastern and Central Europe: Ksenija Makar-Ausperger
- European Union: Danielle Bardelay

- USA: Sidney Wolfe/ Peter Lurie, to be confirmed
- South America: Perla de Buschiazzo

- 13.00** Lunch ☕
- 14.00** Introduction to workshops
- 14.15** Workshops 1 & 2 (to run concurrently)
- Workshop 1*
How to improve communication within and outside
ISDB: newsletters and web site
Moderators: Maria Font and Christophe Kopp
- Workshop 2*
Why take drug costs into account when making
recommendations?
Moderator: Philip Sax
- 15.30** Break ☕
- 16.00** Plenary:
Chair for the afternoon session: Fausto Bodini
Reports from workshops, discussion and endorsement
of actions

THURSDAY EVENING
Dinner in Dubrovnik

FRIDAY 20th

- 9.00** Coffee ☕
Chair for the morning session: José Recalde
Plenary: short presentations
- 9.30** Campaigns on misleading advertising
– Gopal Dabade, Buko-Pharma, Germany
- 9.45** Discussion
- 9.55** Scope of unpublished studies at approval time
– Björn Beermann, Medical Products Agency,
Sweden
- 10.10** Discussion
- 10.20** Producing a bulletin in a country where direct-to-
consumer advertising is legal
– Patricia Logan, PreMeC, New Zealand
- 10.25** Discussion
- 10.45** How bulletins can deal with complementary and
alternative therapies
– Helen Barnett, DTB, UK

- Discussion
- 11.10** Break ☕
- 11.40** Results of the Swedish/French study comparing
ratings on new drugs by two ISDB members
– speaker to be confirmed
- 12.00** Discussion
- 12.15** The International Conference on Harmonization (ICH)
process
– Gianni Tognoni
- 12.35** Discussion
- 13.00** Lunch ☕
- 14.00** Introduction to workshops
- 14.15** Workshops 3 & 4 (to run concurrently)
- Workshop 3*
What should ISDB members expect from regulatory author-
ities in terms of transparency and information about pharma-
covigilance?
Moderator: Wolfgang Becker-Brüser



Workshop 4

How ISDB members can communicate with patients. Sharing experiences on publishing information aimed directly at patients

Moderator: Molly Thomas

15.30 Break ☕

16.00 Plenary:
Chair for the afternoon session: Jan Schuling

Reports from workshops with proposals for future actions, followed by discussion

17.15 Updating the constitution: introduction
Presentation of proposals for revision
Presentation of proposal 1
Presentation of proposal 2

17.40 Discussion

SATURDAY 21th

General assembly

Chaired by Ksenija Makar Ausperger

Anyone can attend the GA but one representative from each full member bulletin can vote.

9.00 Coffee and voting on constitution amendment proposals (secret ballot)

Results of voting

Brief presentations from candidates for election to the committee

10.00 Voting for the new committee (secret ballot)

10.10 Counting of votes
(committee and constitution proposals)

10.20 Results of voting

10.45 Presenting the new committee (a short break while the committee decides on members of the executive committee) and recap on plan for activities for the next 3 years.

11.30 **Close and farewell by Bozidar Vrhovac**

SATURDAY AFTERNOON

Tour by boat to three islands

GUIDANCE FOR EFFECTIVE COMMUNICATION AT THE GA

We want to be sure that everyone attending the GA in September can benefit as much as possible from the meetings. All the sessions will be conducted in English, which of course is not everyone's first language. There is little point in devoting time, human efforts and financial resources unless all attendees can understand what is going on during meetings and discussions. So, we have prepared some friendly advice with the aim of helping everyone to understand and participate in the proceedings. The general guidance is intended for everybody, while the more "specific" guidance is for those who will formally be participating as moderators, speakers or

reporters during the working sessions.

A

General guidance is for speakers, moderators, reporters and all those who care to make themselves understood

Not everybody may understand English as an English-speaking person does.

Not everybody may speak English fluently.

So, if you speak both too fast and in a complex way:

- your audience may not under-

stand what you are talking about

- you can actually discriminate against people who can't understand you properly
- you can discourage participation from those who are reluctant to speak, such as those intimidated by the complexity of your language
- you can discourage contributions from people who feel they have something to say, but they say nothing, being afraid to be engaged in the discussion.

SO, PLEASE, REMEMBER TO SPEAK SLOWLY AND CLEARLY



B

Specific guidance for those involved in a workshop

1 Moderator

A moderator should:

- Keep in mind the general guidance
- Ensure the timetable is observed
- Present the speaker(s) who will set the scene for the workshop
- Ask participants to nominate a reporter
- Explain that the aim of a workshop is to encourage people to talk to one another, rather than to address themselves to the speaker
- Avoid engaging her/himself in the discussion
- Encourage participation from those who are reluctant to speak: a good idea is bad if not said
- Ensure that all participants can say their views
- Keep particular personal or professional views from dominating the discussion
- Adopt a more interventionist style later on in the session, by encouraging attendees to reach a conclusion.

2 Speaker(s)

Speaker(s) should:

- Again, keep in mind the general guidance
- State and illustrate some key-points (2-3) of the topic, in advance (What about posing them as questions?)
- After the speaker has finished, participants could be asked by moderator for any key-point to be added, according to their experience and knowledge
- Key-points should be a “discussion trail”, along which participants try to answer to the stated keypoints.
- Conclusions might be the answers to the questions

3 Reporter

Should follow:

- the general guidance
- Report the conclusions, as answers to the questions.

4 Workshops

We are planning that there may be two workshop groups for each workshop topic depending on the number of attendees. A speaker or moderator or reporter should take into account the proposals coming from each of the two workshop groups, discuss them with both groups and write down a shared proposal to be introduced in plenary as a report with proposals for future actions. Reporting in plenary could be done by the moderator or reporter or speaker.

*[Thanks to Fausto Bodini
(Dialogo sui farmaci)
for putting forward these proposals;
thanks to Andrea Tarr (DTB)
for editing the draft.]*

For full members and recognised correspondents it may concern.

Pay your membership fee!

You probably received a request for your membership fee for 2002. Please pay as soon as possible. ISDB's activities depend on your contribution.

SUMMARY OF ISDB ACCOUNTS FOR 2001

INCOME	BRITISH POUNDS
Membership fees	9912
Bank interest	78
Total income	9990
EXPENDITURE	
Administration (newsletter/telephone – France)	920
Administration (Italy).....	20
Bank charges	128
Travel/accommodation expenses (related to attendance at declaration/ committee meeting November 2001 for: Gita Fernando, Maria Font, Andrew Herxheimer, Dzul Razak, Gianni Tognoni)	2444
Other travel/accommodation expenses Visit to Algeria by chairman	610
Attendance at European Parliament workshop, Luxembourg by chairman	98
Total expenditure	4220
BALANCE	5770
Surplus from previous years	£14,621
Therefore total available at beginning of 2002	£20,391

Prepared by Andrea Tarr, treasurer, 4 March 2002

www.ISDBweb.org

The new ISDB web site is handled by Dialogo sui Farmaci's staff, and a first update was done as scheduled. Please check your particulars in the membership section. The website will reflect our activities and carry important documents.

Information on the next general assembly can be found (registration, accommodation).

Also available: the ISDB positions on regulatory matters

The ISDB European group has taken a number of positions on regulatory matters during the last months (see supplement enclosed).

In the What's new section you'll find:

- the ISDB position about the proposals of the EU Commission regarding drug approvals and pharmacovigilance, delivered to the Economic and Social Committee in February 2002;
- the ISDB position on a proposed EU regulation for better medicines in children, in April 2002.

In the Publications section you'll find:

- the ISDB Declaration on Therapeutic Advance in the Use of Medicines, available in several languages;
- an ISDB communication on "Information to consumers" delivered at the International Conference "European integration and national health care systems: a challenge for social policy" in Ghent (Belgium) on 7-8 December 2001.

Feel free to forward your comments on the site to Maria Font <maria.font@ulss20.verona.it>.

NEWS FROM MOLDOVA

Access to essential drugs for diseases of poverty is a priority for Moldovan people. The huge consumption of metamizole (dipyrone) in that country is an indication that access to appropriate drug information is crucial. Natalia Cebotarenco (DrugInfo Moldova) sent us a report of a workshop held in December 2001 in Chisinau, titled "Massive effort against diseases of poverty in Moldova and access to medicines".

On December 6, 2001, the Ecumenical Pharmaceutical Network, the country's focal point for Newly Independent States (NIS) and DrugInfo Moldova, held a one-day workshop titled "Massive Effort against Diseases of Poverty in Moldova: Access to Medicines." The aim of the workshop was to increase Moldovans' awareness of the range of diseases associated with poverty and to improve access to essential medicines. Participants included parliamentary officials, tuberculosis (TB) and HIV/AIDS experts, church leaders, and officials from the Ministry of Health, Economy and Finance as well as the National Institute of Pharmacy. Also present were staff from TB and infectious diseases hospitals, non-governmental organizations, and the media.

General situation in Moldova

Moldova has a population of about 4.3 million and is situated in Eastern Europe between Romania and Ukraine. Like most of the Newly Independent States, Moldova has struggled with economic and social difficulties since the collapse of the Soviet system in 1991. Among the many problems Moldova now faces are increased poverty and increases

in the incidence of diseases associated with poverty.

One of the biggest problems in Moldova's health care system is the State's inability to buy essential drugs. A poorly conceived and inconsistent drug purchasing policy has made essential medicines inaccessible to most Moldovans.

Moldova's current per capita GDP is \$US315, making it one of Europe's poorest countries. Whilst registered unemployment is only about two percent, the actual number is estimated to be 52 percent. Wages for Moldovans who are employed are low and often irregularly paid. The average monthly salary for public sector employees (including doctors and teachers) is \$US25. A pension averages about \$US10 per month, and in rural areas the State is more than seven months behind in paying pensions. The average monthly rent for a pensioners' apartments is \$US25. Overall, the real value of national income dropped in 2000 to one-fifth of what it was in 1990.

Speaking at the workshop, Mrs Ana Tomcheac, a representative of the UN project "Capacity Building for Poverty Monitoring and Programme Evaluation in Moldova," said that for most people in Moldova, poverty influences both the diseases they suffer and the treatment they receive. Even though there is a wide range of drugs available in Moldova, most medicines are not accessible to the majority of the population.

Treatment of tuberculosis in Moldova

TB morbidity has increased markedly over the past decade. A total of 3000 TB patients were registered in 1996, the total increasing in 1997 to 10,744. In 1998 that figure

increased again to 12,098, the diagnosis of pulmonary TB being assigned to 10,933 of these.

The following year, a further 2,948 cases were registered. Of those, 90 percent (2,648) were newly-diagnosed and 10 percent (299) were relapses. Of the newly-diagnosed cases, 277 (10.4 percent) occurred in prisons.

The highest rate of morbidity is in Chisinau county, but the counties of Ungheni, Soroca and Orhei also have very high morbidity rates.

By January, 2000, there were a total of 12,095 patients in Moldova with active TB (that is, one in 354 Moldovans) and 2,895 with open TB (one in 1,480 Moldovans).

According to the World Health Organisation (WHO), a prevalence of open TB of one in 1,000,000 does not present a threat to the general population, however, the prevalence of open TB in Moldova is currently 689 cases per one million inhabitants.

In 1990, the incidence of TB in children was 5.4 per 1,000,000 and the prevalence 16.5 per million. By 1998, this had increased to an incidence of 9.2 per 1,000,000 and a prevalence 24.4 per million.

One factor which is exacerbating the problem of TB in Moldova is the shortage of anti-TB drugs. At present, patients simply do not receive the necessary treatment, giving rise to an increase in the incidence of TB and multi-drug resistance. Multi-resistant mycobacteria may account for ten to 15 percent of new cases.

In theory, TB hospitals provide free services, but in reality TB patients must pay for their own medication. Unfortunately, anti-TB drugs are too expensive for most of these patients who tend to be poor and are unable to afford to pay drugs as well as food.

In 1996, the government of Moldova implemented a National Tuberculosis Program. At the time of writing, this program has almost completely collapsed with the supply of drugs erratic, drug delivery often inappropriate, and drug use unsupervised.

In 1997, only 38 percent of the

demand for anti-TB drugs was met. The following year only 10 percent of demand was met. In 1999 some areas of Moldova did not receive any money for anti-TB drugs which resulted in most patients being required to pay.

Following consultation with WHO in June 2001, the Moldovan government adopted a new TB program based on the Directly Observed Treatment, Short-Course (DOTS) Strategy. The first stage of the program involves the counties of Chisinau, Orhei and Lapushna. Drugs used in the DOTS program include: isoniazid 100mg and 300mg; rifampicin 150mg and 300mg; pyrazinamide 500mg; ethambutol 400mg and streptomycin 1g.

Professor Ion Vangheli said that the uncertain supply of anti-TB drugs is the main barrier to the effective treatment of tuberculosis and that problems with supply were also affecting the proper implementation of the DOTS strategy. As an example of this problem, he said, funding for the TB program in 2001 was made in two separate instalments: one instalment being made in June, with the second, larger payment being delayed until December. As a result of this, patients in TB hospitals were forced to wait for their medication and the number of untreated TB patients increased.

Funding for anti-TB drugs in 2002 remains uncertain, the best hope being that the international community will donate the appropriate drugs.

Dr Boris Parii, director of the National Institute of Pharmacy, took the opportunity at this point to clarify the rules relating to the donation of medicines to Moldova. He said that Moldova would accept any drugs used to treat diseases associated with poverty. Dr Parii promised that donors would not experience any difficulties with registration or be required to pay any registration fees, provided the medicines:

- are included on the Moldovan Essential Drug List

- are included on the WHO Essential Drug List

- are accompanied by documents confirming their quality, batch number, and manufacturer, and

- have an expiry date of at least one year hence.

DrugInfo Moldova informed participants about a project - DIFAM (German Institute for Medical Mission, Tübingen, Germany to Moldova) - which will provide anti-TB drugs through the Orthodox Church to two TB hospitals - Edinet and Soroca Judet. It was noted that:

Protoirey Vadim Cheibas will be responsible for this project on behalf of the Orthodox Church,

Professor Ion Vangheli and Dr. Maria Cetulean, chief of the Chisinau TB hospital, will be primarily responsible for implementation of the DOTS strategy, and

DrugInfo Moldova, the focal point of the country's Ecumenical Pharmaceutical Network, will supervise the appropriate use of drug donations within the framework of this project.

Access to HIV/AIDS treatment in Moldova

Moldova recorded its first HIV/AIDS case in 1987 and since then 1,436 persons carrying the virus have been registered, including 1,395 Moldovan citizens. Moldova has the fourth highest incidence of HIV/AIDS in the Commonwealth of Independent States, after Ukraine, Belarus and Russia. At least 33 persons have developed AIDS, 23 of them dying as a result. Eighty-three percent of HIV carriers are drug users; 95 percent are aged between 15 and 39 years.

Thirty-eight percent of HIV-infected people are women, and many of these either have, or wish to have children. Professor Galina Russu said that of the 20 HIV-positive women who had given birth in Moldova, only two could afford antiretroviral drugs, which they had obtained from abroad on their own initiative.

Professor Russu said the government of Moldova should be concerned about affordability of the anti-retroviral medicines, especially for the prevention of the transmission of HIV from mothers to their children. Presently, antiretrovirals are not accessible to everyone with HIV/AIDS, partly due to the high cost of the drugs and partly as a result of Moldova's expensive drug registration fees.

Moldova represents a small market for pharmaceutical companies, and international aid organizations are unable to pay the registration fees for their drug donations. Access to anti-retroviral drugs should be the responsibility of the government of Moldova - an issue that has been debated for a long time.

Dr Boris Parii, the director of the National Institute of Pharmacy, repeated the assertion that: "... Moldova is open for any drugs used to treat diseases associated with poverty. Antiretrovirals are more than welcome from any organizations willing to help our republic. Organizations will not be required to pay any registration fees for such medicines. But documentation will be required to confirm quality, batch numbers and country of manufacture of medicines."

The role of the Church

Following the collapse of the Soviet Union and the dramatic increase in the level of poverty in Moldova, thousands of people turned to the newly revived churches for assistance.

Many churches have since taken some responsibility for medical treatment and drug donations in Moldova. Caritas Moldova, the Salvation Army, Caritas Luxemburg, the Baptists, the Evangelic Church and the Orthodox Church provide the greatest assistance to the population, donating food, clothing and medicines. But because churches have only recently become involved in ►►

► health care activities in Moldova, many of their medical staff lack detailed knowledge about key policy areas, including the concept of essential drugs.

The implementation of essential drug policies can assist church health institutions use their resources to manage drugs more effectively and meet high priority health care needs, according to Valentina Buliga, a vice-director of the National Institute of Pharmacy. Ms. Buliga asked churches to treat drug donations with caution, emphasising that donated drugs often lack the necessary documentation. The WHO Guidelines for Drug Donation would be of assistance to churches, she said.

Access to essential drugs

The recognition of health as a fundamental human right brings with it the responsibility of the State to ensure access to health care, including essential drugs. This does not mean that the State should necessarily finance and provide all drugs. A proportion of drug needs - in many countries a very large proportion - may be met through private financing and supply mechanisms. However the State does have a responsibility to ensure that, between the public and private sectors, essential drugs are accessible to everyone.

A table listing the prices of antibiotics was presented at the workshop, illustrating that even a course of antibiotics is unaffordable for Moldovan consumers on a monthly salary of \$US25. For pensioners the situation is even worse. For patients with TB, HIV/AIDS and other communicable diseases the cost to society will be high unless an adequate range of drugs is both financially and geographically accessible to all.

To ensure equitable access to essential drugs, the government will need to provide subsidies to a range of high priority groups, including such as children, and patients with communicable diseases.

Professor Vasili Procopishin suggested that the government should fix the price of essential drugs for two years. Further, he recommended that a special committee be established to compile a register of needy groups, including patients with TB and diabetes, the elderly and orphaned, and that the committee estimate the expense of providing subsidies of at least 50 percent of the cost of essential drugs for these groups.

Drug supply in hospitals

Workshop participants also discussed the role of pharmacists and nurses in the treatment of patients as well as the entrenched misunderstanding of the role of the hospital pharmacist in rational drug choice.

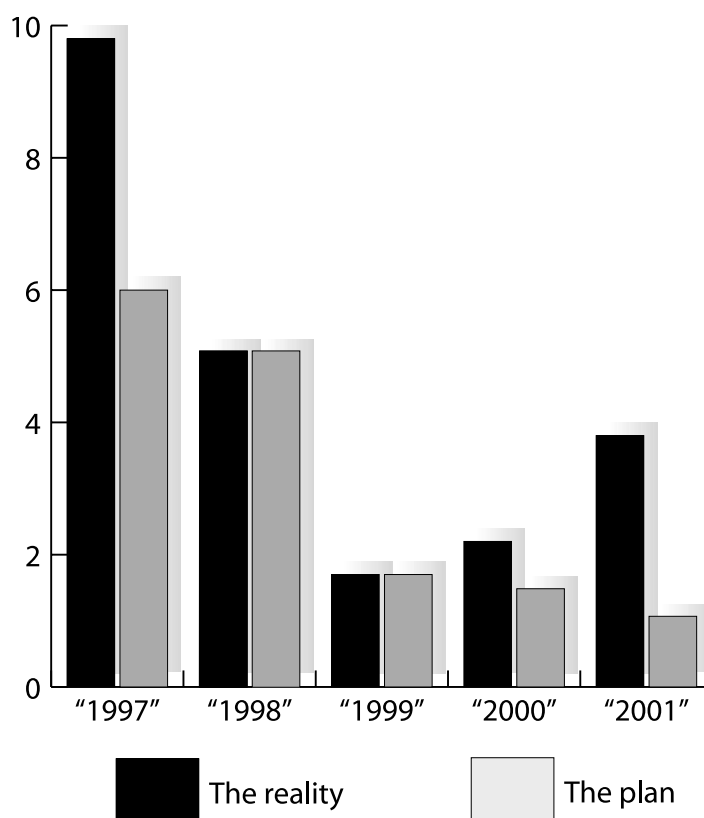
Economic reforms in Moldova have led to the current large number of private pharmacies - 1,200 com-

pared to only 40 state and hospital pharmacies. Because of the low salaries offered by hospitals, there is a shortage of hospital pharmacists with adequate education. Most hospital pharmacies also lack access to the Internet and other sources of information such as Martindale, USPDI and the British National Formulary. Regrettably hospital pharmacists no longer play a meaningful role in the provision of unbiased information about medicines.

Management Science For Health, working with DrugInfo Moldova, initiated a process in 1997 to establish formulary committees in hospitals. A few hospitals that participated in workshops conducted by experts from the Management Science for Health in 1999, have established such committees.

Many state and church hospitals

State budget for drug procurement



would benefit from the support of a formulary committee. In situations where severe budgetary measures are in place, formulary committees could play an important role in optimising available resources.

National drug expenditure

In 1993 the World Bank estimated that the annual cost of Moldova's essential drug requirements was \$US100 million – or, about \$US23 per capita. Compare this with the total budget for the purchase of drugs in 2000 of around \$US2 million (less than 50 US cents per capita). In 2001 that budget increased to around \$US4 million, a figure still representing less than \$US1 per capita.

As an example of the scope of the problem, one of Moldova's biggest hospitals, the Republican Clinical Hospital, received no money at all for the purchase of drugs between May and December, 2001. Overall, including local community finance, the total budget for the purchase of medicines is only 10 to 15 percent of that required.

Metamizole

Key points of the essential drugs policy was related to the new version of the national Essential Drugs List (EDL). According to Dr Tamara Chetrari, of the National Institute of Pharmacy, most participants were not aware of the development of a revised version of the EDL, even though it was adopted in June 2001. Professor Vasili Procopishin added that scientists from the Medical University, who produced the first version of the EDL, were not involved in producing the second version.

The inappropriate process for the development of the EDL is the most likely explanation for the inclusion of a number of potentially harmful drugs on this revised list.

A discussion followed on banning metamizole, which is currently on the new EDL. It was reported that in Moldova 27 different forms of

metamizole are registered, the products originating from Romania (5), Bulgaria (4), Ukraine (4), Germany (2), Estonia (2), Byelorussia (2), Moldova (2), Greece (1), Lithuania (1), Vietnam (1), and Russia (1).

National Institute of Pharmacy director Dr. Boris Parii said it would take a long time to implement a ban on metamizole in Moldova, not only because of the lack of clear data about its side effects, but also because of the popularity of the drug. Dan Zaharia, a representative of the local manufacturer EuroFarmaco, which produces metamizole, complained about the lack of information from the Moldovan registration authorities about the ban. He also drew attention to the absence of recorded cases in Moldova of the adverse effects of metamizole.

Participants agreed on the need to increase awareness in Moldova about the adverse effects of metamizole and the upcoming ban on the drug. Drug-Info Moldova's bulletin "Medex" was suggested as the key medium in which independent information about the banning process should be published.

Consensus Statement

Education about essential drugs and the rational use of drugs is crucial for health care providers in both the State health system and church-run facilities.

There is a need to lobby for the free registration of medicines to treat diseases associated with poverty.

Government authorities should become more aware of the need to make TB and HIV/AIDS drugs available.

Consistent and transparent criteria must be used to develop and adopt a national EDL.

The role of hospital pharmacists in the health care system must be promoted.

The accessibility of essential medicines must be assured. It is therefore necessary to educate health care providers and consumers about the

COLOPHON

Editor: Christophe Kopp

Coordinating Editor:

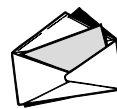
Christine Badiane

Lay-out: Nathalie Froment

The following contributed to this newsletter: Danielle Bardelay (la revue Prescrire), Fausto Bodini (Dialogo su Farmaci), Wolfgang Becker-Brüser (arznei-telegramm), Natalia Cebotarenco (Drugs Moldova), Gita Fernando (Sri Lanka drugs agency), Maria Font (Dialogo sui farmaci), Ksenija Makar-Ausperger (Pharmaca), Andrea Tarr (DTB).

The ISDB Newsletter is sent free of charge to ISDB members and corresponding members.

ISDB



Maria Font,
General Secretary,
ISDB
Dialogo Sui Farmaci
Via Poloni, 1
37122 Verona
Italy

price of drugs and to offer guidance on drug price policies for generic and brand name drugs.

International organizations should be encouraged to donate anti-TB and antiretroviral drugs, and other medicines needed to treat diseases associated with poverty in Moldova.

Policies on essential drugs and drug donations should be implemented in the church health system.

*DRUGINFO MOLDOVA
#2; BOGDAN VOEVOD 2A
CHISINAU, MOLDOVA, 2068
TEL/FAX (3732) 444-012*

ACKNOWLEDGMENT

We wish to offer our thanks to Médecins Sans Frontières and Global Health Council for assistance in conducting this workshop.

HEART FAILURE: VALSARTAN MAY INCREASE MORTALITY

UNFAVORABLE DATA SUPPRESSED

We already underlined the importance of unpublished data and the crucial role played by the FDA website in drawing a more balanced picture of drug effects. We reprint here abstracts and references from papers published on the *Arznei-telegramm* website in January 2002 and in September 2001. The full papers are available at www.arznei-telegramm.de

The recently published Valsartan Heart Failure Trial (Val-HeFT) with valsartan (DIOVAN, PROVAS) for the treatment of heart failure has been managed and evaluated under considerable participation of the manufacturer. Important data that are unfavorable for valsartan, but essential for the assessment, have been submitted to the FDA, but have been omitted from the publication.

In patients with heart failure who in more than 90% of cases take an ACE inhibitor and in 35% of cases a beta-blocker, additionally prescribed valsartan has no effect on overall mortality. The hospitalization rate due to heart failure decreases, while the overall hospitalization rate remains unchanged – probably, because more hospital admissions are caused by adverse drug related side effects.

In patients receiving a beta-blocker, independent of a concomittant therapy with an ACE inhibitor, and in patients who take both a beta-blocker and an ACE inhibitor, valsartan has a significant and clinically relevant adverse effect on mortality.

Mortality is increased nonsignificantly in the group of all patients treated with ACE inhibitors. Thus, an AT-II-blocker is contraindicated in patients with heart failure receiving one or both of the standard treatment drugs. Particularly, combining valsartan with a beta-blocker in patients who do not tolerate an ACE inhibitor – a niche indication for valsartan that is probably intended by the manufacturer – appears questionable upon the data presented.

Whether treatment with valsartan in patients who take neither an ACE inhibitor nor a beta-blocker is in fact better than placebo, will have to be

confirmed by further studies. If 5% of heart failure patients do not tolerate an ACE inhibitor, and of those, another 5% are intolerant of a beta blocker, there would be only 25 out of 10,000 patients for whom valsartan might be indicated.

References

(R = randomised study, M = meta-analysis)

- R 1-** The SOLVD Investigators: *N. Engl. J. Med.* 1991; 325: 293-302
- R 2-** The CONSENSUS Trial Study Group: *N. Engl. J. Med.* 1987; 316: 1429-35
- M 3-** BROPHY, J.M. et al.: *Ann. Intern. Med.* 2001; 134: 550-60
- R 4-** PACKER, M. et al.: *N. Engl. J. Med.* 2001; 344: 1651-8
- R 5-** PITT, B. et al.: *Lancet* 2000; 355: 1582-7
- R 6-** COHN, J.N. et al.: *N. Engl. J. Med.* 2001; 345: 1667-75
- 7-** http://www.fda.gov/ohrms/dockets/ac/01/briefing/3793b1_01_NOVARTIS.pdf
- 8-** http://www.fda.gov/ohrms/dockets/ac/01/briefing/3793B1_03_MEDSTAT.pdf

MANIPULATION OF DATA IN FAVOUR OF COX-2-INHIBITORS IN CLASS AND VIGOR

Following the publication of two large studies VIGOR* and CLASS* of the selective COX-2 inhibitors rofecoxib (Vioxx) and celecoxib (Celebrex), doubts remained regarding safety advantages of these drugs (see also a-t 2000; 31: 107 and 2001; 32: 35-6). Now it has become clear that in both studies essential risk data were withheld from publication.

(...) Both studies publicly reported only the more advantageous results, while the complete data pool showing less favourable results was reported to the FDA only. In our view, this strategy was used to provide the manufacturers with a timely advantage in order to establish their products on the market. (1) The obvious commercial interests reflected in VIGOR and CLASS by tampering with scientific results and disregarding safety concerns for patients, undermine confidence in the seriousness and scientific quality of all study data presented to the public.

1- GOTTLIEB, S.: *BMJ* 2001; 323: 301

NEWS FROM SRI LANKA

LUNDBECK PLAYS FOUL

Gita Fernando, Secretary of the Drug Evaluation Sub Committee in Sri Lanka, reports on the unethical behaviour of Lundbeck, the Dane drug company.

Deanxit is a combination of flupenthixol and melitracen manufactured by Lundbeck, Denmark. Flupenthixol is indicated mainly for treatment of depressive illness whereas indications for melitracen are dubious. An application for registration of Deanxit was submitted to the Drug Regulatory Authority (DRA) of Sri Lanka in March 1997 by Lundbeck, Denmark through their local agents. A free sales certificate issued by the Danish drug administration was submitted along with the application as required by the DRA. A free sale certificate indicates that a drug is manufactured and sold in the country of manufacture. This application also contained a document (1993) which stated that Deanxit is registered in 20 countries including Denmark.

The application was sent by DRA to the Drug Evaluation Sub Committee (DESC) to ascertain whether Deanxit could be registered. The registration of Deanxit was rejected by the DESC in July 1997 as it was a combination of a known and unknown product which had not been registered by reference drug regulatory authorities in countries such as UK, USA, Australia, New Zealand, the Netherlands and Scandinavia. The DESC relies on these reference regulatory authorities to get information mainly on new chemical entities. Following the first refusal of registration, Lundbeck sent a new updated list (1997) of 25

countries where Deanxit was registered but surprisingly Denmark was not on this list!

In September 1997 Lundbeck had appealed to the DRA to reconsider registration of Deanxit enclosing a report on the drug written by their own staff. This report did not indicate any clinical trials. Some of the references were incomprehensible as they were not in English, and most of the documents were not published in scientific journals. However, the application was sent for evaluation by a psychiatrist who also rejected Deanxit (September 1998). The reasons given for rejection were as follows:

- Combination product, hence difficulties in dosage/side effects.
- Melitracen is practically unknown.
- Sufficient antidepressants / antipsychotics available in the country.
- Inadequate substantiation of claimed indications of Deanxit.

It was discovered later that Lundbeck had never applied for sale of Deanxit to the Danish Medicines Agency to get approval for sale of Deanxit in Denmark. It was approved only for export. Lundbeck had not applied for sale of the product in Denmark as Denmark was known to be very restrictive regarding combination products and comprehensive documentation on efficacy and safety. However, when a drug is approved for export, only details of manufacture and basic assay of ingredients are evaluated.

In 1999 January Lundbeck invited some psychiatrists to a meeting at a posh hotel in Colombo to get their support for Deanxit registration. But none of the psychiatrists

had been informed that DRA had rejected registration twice, nor that the drug was not approved for sale in Denmark. Following this meeting a letter was sent by Lundbeck to the DRA enclosing written declarations of support from some psychiatrists regarding registration of the drug. In January 1999 Deanxit was registered on the basis of a unilateral decision by the Director of Medical Technology and Supplies of the Ministry of Health, disregarding the earlier decisions of the DESC and approved Deanxit for sale in Sri Lanka.

News from Eritrea

The third edition of the Eritrean National List of Drugs was published in 2001.

It is published by the ministry of health.

For more details you can contact Embaye Andom, editor of *Drug Bulletin* and Head of the Drug Information Unit at the Department of Pharmaceutical Services.

Tel.: 291 1 102297

Fax.: 291 1 122899

ISDB EUROPEAN MEMBERS HAVE LAUNCHED A LOBBYING CAMPAIGN

A revision of pharmaceutical legislation is underway in the European Union. The proposed legislation is more business-oriented than ever. It involves systematic acceleration of marketing approvals, removal of the 5-yearly renewal of approvals, prolongation of data protection, direct-to-consumer advertising of prescription medicines (disguised as disease education). It leaves in a black box all matters related to pharmacovigilance. It doesn't plan for the removal of the mutual recognition procedure, which is a totally secretive procedure. Above all, the proposed legislation does not improve transparency and accountability of the EMEA towards health professionals and the public, which is in conflict with an EU Regulation on public access to documents and the Charter of Fundamental Rights of the EU citizens.

ISDB and the following ISDB members, together with closely related organisations have started a lobbying campaign or made amendments to the proposed legislation.

– **In Germany:** BUKO Pharmakampagne Pharma-Brief, Arzneitelegramm, Arzneimittelbrief.

– **In Italy:** Dialogo sui Farmaci, Informazioni sui Farmaci, Ricerca & Pratica, Mario Negri Institute.

– **In Sweden:** KILEN - Consumer Institute for Medicines and Health,

– **In Spain:** Boletín Terapéutico Andaluz, Buletí Groc, Agencia de Cooperación Internacional Farmacéutica.

– **In France:** la revue Prescrire (see supplement enclosed).

– **In Belgium:** Folia Pharmaco-therapeutica, Association Internationale de la Mutualité.

– **In the UK:** Social Audit.

Health Action International is strongly involved in this campaign (see www.haiweb.org)

If you are already involved in a similar action or if you want to join in, feel free to contact Christophe Kopp (christophe.kopp@wanadoo.fr)

La revue Prescrire
has just launched
its website at

www.prescrire.org

La revue Prescrire

The international non proprietary name of amfebutamone has been discretely changed to bupropion

– **The INN has been changed for reasons that are unclear.**

The international non proprietary name amfebutamone was adopted and recommended by WHO in 1974. It had the merit of reminding prescribers that this drug substance has a structure similar to that of amphetamine derivatives (1).

In 2001, shortly after our review article on amfebutamone went to press (2), we received a list of amendments to the WHO list of INNs, in which "amfebutamone" had been replaced by "bupropion", the common English name (3).

This type of change to a radically different INN is rare, yet no explanation was offered. Strangely, this measure does not apply to all drugs in this group. For example, amfepramone, an amphetamine derivative close to amfebutamone, has kept its name (a), even though the English-speaking community usually calls it diethylpropion.

At the time of writing (1 February 2002), WHO has not yet answered our request for information on the reasons (administrative or scientific) that led them to replace an informative INN that had been in use for 27 years.

We received a letter dated March 18 2002 from the World Health Organisation (6). It described in great details all the steps leading to the change in the INN but failed to explain the rationale behind it. So we've asked again but no reply yet (15 June 2002).

[Taken from *la Revue Prescrire* March 2002; **22** (226): 191]

a- Amfepramone was among the appetite suppressants suspended because of the risk of heart valve disease and pulmonary hypertension (ref 4,5).

Selected references from Prescrire's document watch.

- 1- Prescrire Rédaction "Le segment-clé du mois: -amfe-" *Rev Prescr* 2001; **21** (221): 671.
- 2- Prescrire Editorial Staff "Amfébutamone" *Prescr Int* 2001; **10** (56): 163-167
- 3- "Recommended INN: list 45. Amendments to previous lists" *WHO Drug Information* 2001; **15** (1): 54.
- 4- Prescrire Rédaction "Appetite suppressants: valve disease and pulmonary arterial hypertension" *Prescr Int* 2000; **9** (45): 211.
- 5- "Amfepramone: new cases of primary pulmonary hypertension" *WHO Drug Information* 2001; **15** (1): 23.
- 6- World Health Organisation/Quality and Safety of Medicines "Lettre à la revue Prescrire" March 18 2002.