



# International Society of Drug Bulletins Newsletter

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*The International Society of Drug Bulletins (ISDB) is a worldwide network of publications on drugs and therapeutics that are financially and intellectually independent of the pharmaceutical industry.*

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## President's report

Joe Collier [jcollier@sghms.ac.uk](mailto:jcollier@sghms.ac.uk)

It was a great honour to be elected president of ISDB at the General Assembly in Dubrovnik last September. The elections took place at the end of the meeting, so there was little time for myself, and the other members of the new committee, to meet one another, and no time for the committee to discuss ideas with other colleagues. With this in mind, perhaps the first thing I should do as president is to introduce myself.

I am the editor of the UK *Drug and Therapeutics Bulletin (DTB)*, a post I have held since 1992. Prior to that I had, since 1973, been deputy editor of *DTB* (under Andrew Herxheimer), having joined the bulletin in 1969. During my tenure, editorship of *DTB* has been a part-time appointment, nominally one day per week. For the rest of my week—when not faxing, phoning or emailing the ISDB office—I work as a clinical pharmacologist, consultant physician and Professor of Medicines Policy at St George's Hospital and Medical School in South London.

Immediately after my election in Dubrovnik I did have a moment to address members present.

My first priority was to thank Christophe Kopp, the outgoing president, and his committee for all their hard work and endeavour steering ISDB through some difficult years. Under their stewardship ISDB made some very important advances.

I then, very briefly, set out my vision for the society. It is time, I said, to nurture our roots. We must endeavour to help strengthen the work of established bulletins and to bring in to our membership new bulletins whenever the opportunity arises. To this end we must create a vibrant, credible, integrated and supportive network.

I went on to say that, in my view, the primary role of ISDB is to empower bulletins to influence local practice—how 'local' would depend on ad hoc links forged between members.

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*Apart from official reports of the society, the views expressed in this newsletter are solely those of the individual authors and do not necessarily reflect the position of the society.*

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During this next three years, I do not see it as a priority of the ISDB committee or the ISDB president to lead worldwide 'political' campaigns. I plan that the byword for my presidency will be *consolidation*.

In keeping with these ideals, and to discover what others thought of my proposals, I have been keen to meet with representatives from as many bulletins as possible. For me, it is important to learn first hand what members want from ISDB, and to discuss ways of running the society in an open and transparent way to the benefit of all.

So far I have had face-to-face meetings with 8 editors/managers (4 in Australia and New Zealand, and 4 in Germany), and I am planning to meet a further 20 before 2003 is over. To help in this endeavour, may I invite any member visiting London to contact me so that we can meet to discuss ISDB business.

It is clearly important for you to know how I plan to work as president. ISDB is a complex organisation, has a worldwide membership, and relies on a tiny budget. For practical reasons the day-to-day business will be done by myself, the secretary and the treasurer (informally known as the executive group). The executive group will meet three times each year—twice by ourselves and once with the full committee (with some members possibly attending through a phone or video link).

Before each executive group meeting, the proposed agenda will be circulated to all members of the committee for comments and suggestions. After the meeting, the minutes and any proposals will be sent to them for ratification. Key approved minutes will then be circulated to all ISDB members by email, with the full minutes published subsequently in the newsletter (see page 15 for the minutes of our December 2002 meeting).

Apart from myself, the executive group is made up of Josef Tukker as secretary and Andrea Tarr as treasurer (all positions required in our constitution). Josef is the editor-in-chief of *Geneesmiddelenbulletin* in the Netherlands and his appointment was straightforward—he was elected to the post

by the committee in Dubrovnik. At the time, nobody from the committee was prepared to stand as treasurer. As a result I asked, during my inaugural address, whether Andrea Tarr, who had been treasurer of ISDB for the previous 4 years, might be permitted to continue in the post for 3 months as an interim measure. This was agreed.

Towards the end of the 3 months, volunteers for treasurer were again sought from the committee, with a note that Andrea, who works as an associate editor at *DTB*, would be prepared to continue if names did not come forward. No volunteers were

forthcoming, so at the beginning of this year Andrea was formally appointed as treasurer and coopted on to the committee.

Andrea has also been taken on as ISDB coordinator, working in this capacity for half a day each week. Other appointments made by the committee were Maria Font, as webmaster, and Mary Hemming, as editor of this newsletter.

Enough from me. I promise that my next report will be rather briefer. But before closing, may I repeat what a great honour I feel it is to act as your president, and remind you that my door at *DTB* is always open to you.

## Secretary's report

Josef Tukker [j.tukker@geneesmiddelenbulletin.nl](mailto:j.tukker@geneesmiddelenbulletin.nl)

### Bids to organise and host the 2005 Workshop and General Assembly

All ISDB members are invited to make a bid to organise and host the next Workshop and General Assembly, which will be held in 2005 between June and September.

ISDB is a worldwide organisation. As the majority of meetings have so far been held in Europe, the committee would like a country outside Europe to host the next assembly—preferably a country with visa rules that are easy to comply with, especially for participants from developing countries.

Bids should include the following information:

- venue location
- features of the venue
- venue accessibility (by air, train and car)
- suggested accommodation (including proximity to the venue)
- experience of the local staff in organising such a meeting
- estimated costs (preferably in \$US).

We would like to receive all bids by 1 August 2003. The committee will determine the successful bid at its meeting in September 2003, and the decision will be published soon after.

### Please check your contact details

Since last year we have had an easily accessible website ([www.isdbweb.org](http://www.isdbweb.org)), which will be updated on a regular basis.

The website lists the contact details of ISDB members and recognised correspondents under a link titled 'Members'. At the moment some of these details are incorrect or incomplete.

I would like to ask all members and correspondents to verify their details and report any corrections to me by the end of April 2003.

Please supply the following information:

- name of organisation or publication
- editor or contact person
- postal address
- telephone and facsimile numbers
- email address
- website address.

I will ensure this information is transferred to the webmaster, Maria Font, and the newsletter editor, Mary Hemming.

# 2002 Workshop and General Assembly

Bozidar Vrhovac and Ksenija Makar-Ausperger, *Bilten o lijekovima* and *Pharmaca* [vrhovac@kbc-zagreb.hr](mailto:vrhovac@kbc-zagreb.hr)

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The 2002 ISDB Workshop and General Assembly was held in the beautiful town of Dubrovnik on the Adriatic coast of Croatia, the country of one of the cofounders of ISDB, Bozidar Vrhovac. The meeting was organised by the Croatian journals *Bilten o lijekovima* and *Pharmaca*, the venue being the International Centre of Croatian Universities. This is located in the old part of Dubrovnik and has recently been rebuilt after having been destroyed in the civil unrest of the early 1990s.

Sixty-four people attended the meeting, representing 40 drug bulletins and journals. Bearing in mind that ISDB has 55 full members, the attendance at the meeting was very pleasing. Along with ISDB funding, some Croatian institutions and organisations (not industry!) also gave financial support.

Since the last General Assembly, 11 new members have been accepted, 8 as full members and 3 as recognised correspondents. In the poster session, 24 bulletins displayed their publications and 10 presented a poster describing their activities. The very influential *Arznei-Telegramm* presented its new edition, *Arzneimittelkursbuch 2002/2003*, a critical presentation of every drug in the very abundant German market.

The 2-day professional program covered important questions that arise in the day-to-day practice of ISDB members. For those who were unable to attend, more details about the program can be obtained from the authors of this report.

## Part 1: Professional program, 19–20 September

The program for the first two days of the meeting consisted of reports from the outgoing executive group, short presentations from various regions of the world, plenary sessions and workshops.

### Reports from the 1999–2002 executive group

The outgoing president, Christophe Kopp, gave a detailed report on the activities of ISDB over the last 3 years, describing the openness of the organisation to new ideas, and its cooperation with new members and other organisations such as WHO. He also stressed the importance of transparency in drug regulatory agencies. Andrea Tarr presented the 2002 Financial Report (see page 14), which showed satisfactory results.

Time constraints did not allow the secretary, Maria Font, to give more than a very brief outline of all the various activities she undertook during the previous three years—maintaining the ISDB website, facilitating communication between members, preparing committee meetings, and so on.

### Short presentations

In this section a number of speakers from around the world presented news from their respective regions.

### Plenary sessions

Gopal Dabade from BUKO Pharma-Kampagne in Germany spoke about 'Campaigns on misleading advertising'. He listed examples where pharmaceutical companies had exhibited double standards by advertising their products in a completely different way in developing versus developed countries.

Björn Beermann from the Medical Products Agency in Sweden presented a discussion on the 'Scope of unpublished studies at approval time'. Speaking from the position of someone working within a regulatory body, he outlined the difficulty in finding unpublished, especially negative, studies that would allow fully informed decisions to be made at the time of drug approval.

Patricia Logan from PreMeC (National Preferred Medicines Centre) in New Zealand highlighted the importance of producing an unbiased bulletin in a country where direct-to-consumer advertising of prescription drugs is legal. Direct-to-consumer advertising is currently allowed in the US and New Zealand, but there is a push from the pharmaceutical industry to introduce this practice into many other countries.

*Some of the attendees at the 2002 Workshop and General Assembly in Dubrovnik, Croatia*



Helen Barnett from the *Drug and Therapeutics Bulletin* in the UK discussed how bulletins might deal with complementary and alternative therapies. Helen stressed that this kind of therapy is increasingly popular in many regions of the world and that, despite the fact that evidence of efficacy exists in only a few diseases, it should not be ignored.

## Workshops

Four workshops gave participants the opportunity to explore areas of particular interest.

### *Workshop 1. How to improve communication within and outside ISDB*

The participants in this workshop concluded that ISDB's main goals should be to:

- facilitate informal contacts, visits and regional meetings
- establish an electronic mailing list, restricted to members only, which would provide information on policies, new drugs and warnings, and technical expertise.

### *Workshop 2. Why take drug costs into account when making recommendations?*

To prescribe appropriately, doctors need reliable data on efficacy, safety, availability and price of drugs. Price is often artificial, independent of real cost and varies according to the marketing decisions of the industry. The question was: 'What can ISDB do?'

Suggested possibilities were:

- to use articles to demystify pricing decisions and costs of research and development
- on a micro level, for each ISDB member to encourage prescribers to think about the best drug for individual patients based primarily on evidence of relative efficacy, safety, quality and convenience.

### *Workshop 3. What should ISDB members expect from regulatory authorities in terms of transparency and information about pharmacovigilance?*



*Danielle Bardelay and Gianni Tognoni*

### *Workshop 4. How ISDB members can communicate with patients. Sharing experiences on publishing information aimed directly at patients.*

There was lively discussion in both of these workshops and participants were able to report on experiences in their own countries and gain an insight into what happens in other parts of the world.

## Val-HeFT (valsartan in heart failure) trial

A special meeting was held to discuss issues surrounding the Val-HeFT trial.

*(A report on this discussion will be published in the next issue of the newsletter.)*

## Part 2: Sixth General Assembly, 21 September

The third day of the meeting in Dubrovnik was devoted to the General Assembly—the sixth since the society was established. Two items were on the agenda:

- proposals for change to the constitution and rules
- election of the new committee.

Representatives of the 23 bulletins present, plus 2 proxies, participated in voting.

Members were reminded that according to the 17-year 'old' constitution, 'Resolutions to change the Articles or Rules of the Society and to dissolve the Society shall require at least a three-quarters majority vote of a General Meeting and shall be taken by secret ballot.'

## Proposals for change to the constitution and rules

Two proposals for change were presented for discussion. Proposal A had been prepared by the 1999-2002 committee and proposal B by *La Revue Prescrire*. There was no intention in either proposal to diminish the independence of the society and its members. The main difference between them was the extent of the changes being advocated. Proposal A recommended changes to some of the articles in the constitution, while proposal B recommended that the constitution be left as it is with just new rules being added to the existing rules. For the information of members, the main points in the proposals are summarised over the page.

## Proposal A

### 1. Definition of a drug bulletin

The definition in the constitution is: 'A periodical concerned with the promotion of rational drug therapy and published at least four times a year.'

It was proposed that this be amended to: 'A serial publication concerned with the promotion of rational therapy. Serials should be published at least four times a year, or less frequently if agreed on by the committee. Publications can be in a printed form, or electronically on CD-ROM or online.'

### 2. Definition of good quality information

Point (a) of the current definition includes the statement that 'it is scientifically valid and clarifies current scientific consensus and distinguishes what is established from what is not.'

It was proposed that this be amended to state that 'it is based on appraisal of the best available evidence and includes references to that evidence wherever appropriate.'

### 3. Official language

The current wording regarding language states that: 'The Society's official languages are English, French and Spanish. The English version of the Articles and Rules of the Society is definitive.'

The proposed amendment was: 'The language for communication of Society business is English.'

### 4. Member status

An organisation or individual sympathetic to the purposes of the society but not qualified to be a member is currently termed a 'recognised correspondent'.

This proposal recommended that the terminology be changed to 'associate member'.

### 5. Consumer bulletins

The possibility of a drug bulletin produced solely for consumers was not foreseen in the original constitution. To cover such an event it was proposed that the following rule be added: 'A bulletin aimed at consumers alone may not be a Member of ISDB but may be an Associate Member.'



Rokuro Hama, Mary Hemming and Bozidar (Darko) Vrhovac

## Proposal B

This proposal was based on the notion that only minor adjustments to the operation of the society were required and that these could be achieved by the addition of some new rules. It was proposed that the following rules be accepted:

#### 1. Consumer bulletins

*'A bulletin aimed at consumers can be a full member if it is in line with Articles 2 and 5 of the Constitution, and if it helps the users of the information to clarify current scientific consensus and distinguishes what is established from what is not.'*

#### 2. Electronic bulletins

*'A bulletin published exclusively on the Internet can be a full member if it fulfils the requirements of Articles 2 and 5 of the Constitution.'*

#### 3. Translation and reprint of bulletin articles among members

*'Unless otherwise stated, ISDB full member bulletins can translate or copy free-of-charge articles of other full member bulletins. Bilateral agreement between translated and translating bulletins must always be made beforehand. And the originator publication must be explicitly mentioned, with date of initial publication.'*

The requirement for a three-quarter majority of votes proved to be an insurmountable obstacle as there were insufficient votes for

any of the proposed changes to the constitution to be approved.

## Election of the new committee

As specified in the constitution, the committee is the executive body of the society and is elected every three years.

Those newly elected to the committee in Dubrovnik were: Joe Collier (UK), Gita Fernando (Sri Lanka), Etzel Gysling (Switzerland), Rokuro Hama (Japan), Walter Thimme (Germany), and Josef Tukker (The Netherlands).

Those re-elected (having served on the previous committee) were Maria Font (Italy), Mary Hemming (Australia), Ksenija Makar-Ausperger (Croatia) and José Maria Récalde-Manrique (Spain).

After the election, the new committee met briefly. Joe Collier was elected as president and Josef Tukker as secretary. The position of treasurer was not filled and, during a brief address to the society, Joe Collier sought permission for Andrea Tarr, the treasurer for the outgoing committee, to continue as treasurer for a further 3 months, by which time the post could be filled definitively. This was agreed.

# The gefitinib story

Rokuro Hama and Keiko Sakaguchi, *Kusuri-no-Check (Check your pills to save your life)* [gec00724@nifty.ne.jp](mailto:gec00724@nifty.ne.jp)

Gefitinib (Iressa, ZD1839, AstraZeneca Japan) was approved by the Japanese Ministry of Health, Labor and Welfare (MHLW) in July 2002 for the treatment of inoperable or recurrent non-small cell lung cancer (NSCLC). In Japan, up until the end of January 2003, approximately 23 500 people had received gefitinib and 183 deaths had been attributed to the drug. Acute lung disease and/or interstitial pneumonitis were implicated in 173 deaths. In this article we shall give a brief description of gefitinib, an outline of the experience with this drug in Japan and in Western countries, and also our opinion on what should be learnt from this story.

## Mechanism of action

Epidermal growth factor receptor (EGFR) is a cell surface receptor. Tyrosine kinase acts on this receptor within the cell to regulate cell proliferation and survival. Inactivation of EGFR by tyrosine kinase inhibition induces apoptosis (cell death), and reduces angiogenesis and metastasis of cancer cells.<sup>1,2</sup>

During anticancer therapy research, AstraZeneca researchers noted that:

1. there was an increased EGFR-mediated drive in a variety of solid tumours (eg NSCLC, breast cancer)
2. excessive activation of EGFR on the cancer cell surface was associated with advanced disease and a poor prognosis in cancer patients.

Inactivation of EGFR therefore became a target for anticancer therapy. AstraZeneca screened 1500 EGFR-tyrosine kinase inhibitor (TKI) derivatives and developed the orally active gefitinib as the most selective inhibitor.<sup>3</sup>

## Effect on normal cells

AstraZeneca has stressed gefitinib's EGFR-TKI selectivity and its efficacy on experimental tumour models.<sup>1-3</sup> However, they have not adequately addressed the potentially harmful effects on normal tissue and injured noncancer cells.

Almost all cells have EGFRs.<sup>4</sup> So gefitinib not only inhibits the growth of cancer cells but also inhibits physiological replacement of normal cells, particularly after injury when recovering tissues require more epidermal growth factor.

This effect has been demonstrated in animal models. Studies in mice and rats with

deficient levels of EGFR have shown impaired epithelial development in several organs, including skin, lung and gastrointestinal tract<sup>4</sup>, severe bleeding and weight loss in newborn rats with laboratory-induced necrotising enterocolitis<sup>5</sup>, and delayed corneal wound healing.<sup>6</sup>

## Animal toxicity studies

Six-month toxicity studies in dogs revealed an increase in hepatic necrosis after gefitinib was given at doses of 5 mg/kg/day, which approximates the clinical dose in humans. When doses of 15 mg/kg/day were given after 10 days at 25 mg/kg/day, relative lung weight and white blood cell counts in dogs increased dose-dependently<sup>3</sup>, indicating lung inflammation that was possibly induced by gefitinib.

In 6-month rat studies, 4 of 60 rats died after being given gefitinib at a dose of 25 mg/kg/day for 8 weeks followed by 15 mg/kg/day for 4 months.<sup>3</sup> The rats were shown to have renal papillary necrosis, liver necrosis and other lesions. These findings were considered to be consistent with the mechanism of action of gefitinib.<sup>3</sup>

It was reported recently in the Japanese press that AstraZeneca did not submit the

results of a series of animal experiments that showed gefitinib increased bleomycin-induced lung toxicity (alveolar damage and fibrosis).<sup>7</sup> This is currently being investigated by the MHLW.<sup>8</sup>

## Clinical Trials

### IDEAL 1 and IDEAL 2

Results of two randomised double-blind phase II trials (IDEAL 1<sup>9</sup> and IDEAL 2<sup>10</sup>) were presented at the American Society of Clinical Oncology (ASCO) meeting in May 2002.

IDEAL 1 (AstraZeneca Study 16) enrolled 210 patients with locally advanced or metastatic NSCLC who had previously received at least one chemotherapy regimen containing platinum.

IDEAL 2 (AstraZeneca Study 39) enrolled 216 patients (mostly Caucasians) with locally advanced or metastatic NSCLC who had previously failed at least two prior chemotherapy regimens containing platinum and docetaxel therapy. In both trials, patients received gefitinib orally at a dose of either 250 mg daily or 500 mg daily. Response and survival rates are shown in Table 1 below.

**Table 1. Tumour response rate and median survival in patients treated with gefitinib after previous treatment with platinum-based chemotherapy**

	IDEAL 1 (Study 16)		IDEAL 2 (Study 39)	
	250 mg/day	500 mg/day	250 mg/day	500 mg/day
Objective tumour response rate	18.4%	19.0%	11.8%	8.8%
Median survival (months)	7.6	8.1	6.1	6.0

A subsequent evaluation of Study 16 by the Japanese Pharmaceutical and Medical Devices Evaluation Centre showed that the response rate in Japanese patients (23.5% in both 250 mg and 500 mg arms) was higher than in non-Japanese patients (5.8% in 250 mg arm, 9.3% in 500 mg arm). Although the reason for this difference is not entirely clear, the less intensive and shorter duration of chemotherapy regimens often used in Japanese patients may influence the response to subsequent therapy.

### Adverse reactions

In Study 39 the most frequent adverse events in patients receiving 250 mg gefitinib daily were diarrhoea (57%), rash (48%), asthenia (28%), dyspnoea (28%), nausea (27%) and acne (26%).<sup>11</sup>

The mortality rate in this study due to adverse events was reported as 5.1% (11/216).<sup>3,11</sup> However, another 4 deaths due to adverse events—pneumonia (1), acute respiratory distress syndrome (ARDS) (1), dyspnoea (2)—were described in a note outside the relevant table. The true mortality rate due to adverse events was therefore almost 7% (15/216).

Serious adverse events such as ARDS and/or pneumonia or pneumonitis (or acute lung injuries) were seen in 55 of the 216 patients (25%) in Study 39 and in 39 of the 107 Caucasian patients (36%) in Study 16. Of these, 15 patients (6.9%) in Study 39 and 4 Caucasian patients (3.7%) in Study 16 died due to adverse events.

In one of the phase I/II trials (AstraZeneca Study 11), 9 of 69 patients (13%) died due to an adverse event. Of these, 7 had respiratory tract complications: pulmonary insufficiency (2), pneumonia (2), bleeding from respiratory tract (2), and ARDS (1). Of the 9 deaths due to adverse events, gefitinib had been withdrawn in 5 of the patients, but none of these events were classified as drug-related.

### INTACT 1 and INTACT 2

Results of two large randomised, double-blind, placebo-controlled, phase III trials in chemotherapy-naïve patients with advanced

NSCLC were presented at the European Society for Medical Oncology Congress in October 2002.<sup>12,13</sup>

Gefitinib (250 mg/day or 500 mg/day) or placebo was combined with gemcitabine and cisplatin in INTACT 1 (1093 patients)<sup>12</sup> and with paclitaxel and carboplatin in INTACT 2 (1037 patients).<sup>13</sup>

Neither study showed an improvement in response rate or survival benefit when gefitinib was added to standard treatment.

## Pharmacokinetics

Gefitinib is mainly metabolised by liver CYP3A4. CYP3A4 activity varies more than 40-fold between individuals.<sup>14,15</sup>

Subsequently, there is wide (30- to 100-fold) interindividual variation in maximum concentration and area under the curve values after repeated gefitinib dosing.<sup>3</sup> Time to maximum concentration (T<sub>max</sub>) in cancer patients varied from 1 to 24 hours and elimination half-life varied from 10 to 90 hours in healthy volunteers and patients.<sup>3</sup>

## Japanese experience

Gefitinib was approved on 5 July 2002 in Japan, five months after the application was submitted by AstraZeneca.

On 15 October 2002, the Japanese MHLW issued a 'yellow letter' alerting prescribers that the use of gefitinib had been linked to 13 deaths. More detailed adverse effect warnings were also imposed at this time.

However, the mortality rate continued to rise, with 124 deaths due to adverse reactions to gefitinib notified by 13 December 2002. Stricter safety measures were announced by the MHLW on 26 December 2002. These measures were recommended by a panel, comprising experts in medicine and pharmacy, which had been convened to examine the safety of gefitinib.

The new measures require that:

- informed patient consent must be obtained before gefitinib is administered
- gefitinib must only be prescribed by doctors experienced in treating patients with lung cancer

- patients must remain in hospital for four weeks after the commencement of therapy
- doctors must exercise caution in using gefitinib in patients who have a history of interstitial pneumonitis or other lung diseases.

In February 2003, AstraZeneca Japan announced that the number of deaths as a result of adverse reactions to gefitinib in Japan had reached 183 by 31 January 2003.<sup>16</sup> Approximately 23 500 patients had received gefitinib in Japan by this date, and there had been 644 adverse reaction reports. Of these, acute lung disease and/or interstitial pneumonitis were implicated in 473 cases and, of these, 173 patients had died.

AstraZeneca Japan claims that the safety measures introduced by the MHLW on 26 December 2002 have effectively decreased the case mortality rate but the cumulative mortality rate continues to rise.

### Case reports

The following cases were presented to the Japanese panel considering the safety problem of gefitinib in late 2002.<sup>8</sup>

**Case 1.** A woman in her sixties was admitted with progression of lung cancer. Three weeks after admission, treatment with gefitinib was commenced. Her lung cancer responded well and her tumour decreased in size within one week, but the next day she had diarrhoea and dyspnoea. Typical diffuse opaque appearance on the chest X-ray was found and gefitinib was withdrawn. She failed to improve with oxygen and corticosteroid pulse therapy. She died 8 days after the withdrawal of gefitinib from multiorgan failure involving lung, gastrointestinal tract, liver, kidneys and heart.

**Case 2.** An ambulant woman in her seventies with NSCLC was admitted to hospital and gefitinib therapy was initiated the next day. Seven days later, the woman complained of dyspnoea and a chest X-ray indicated interstitial pneumonitis. Gefitinib was withdrawn and she was treated with corticosteroids, but she died later that day.

**Case 3.** A man in his seventies with severe congestive heart failure experienced abdominal discomfort the evening after commencing gefitinib. On day 3, he developed an ileus and gefitinib was withdrawn. However, severe hypoxaemia and pulmonary symptoms progressed. He died one week after the withdrawal of gefitinib with multiorgan failure involving the lungs, gastrointestinal tract, and kidneys. The elimination of gefitinib by CYP3A4 liver and intestinal enzymes may have been compromised in this patient as a result of his severe congestive heart failure.

The panel noted that of the 17 patients who experienced adverse symptoms within one week of commencing gefitinib, 13 (76%) died.

### Published case reports

An article published in *The Lancet* in January 2003 described four Japanese patients with advanced NSCLC who developed severe acute interstitial pneumonia in association with gefitinib.<sup>17</sup> Two patients recovered but the other two died from progressive respiratory dysfunction. The authors concluded that gefitinib induces pulmonary toxic effects, especially in patients with pulmonary comorbidities.

### AstraZeneca response

AstraZeneca has queried the association between gefitinib and the deaths in Japan. A spokeswoman from their London headquarters said:

ILD [interstitial lung disease] has been observed in patients, but causality hasn't been established. The problem with ILD is that it's a well-known phenomenon in patients that have advanced non-small cell lung cancer, and it is associated with other anticancer treatments such as chemotherapy and radiotherapy. We believe that the benefits of the drug far outweigh the potential risks.<sup>18</sup>

### Independent view

The two independent drug bulletins in Japan—*The Informed Prescriber* and *Kusuri-no-Check*—have published widely on this issue and have helped to alert prescribers,

other health professionals and patients to the adverse drug-related effects that have occurred with gefitinib. Such information has not been forthcoming from the drug company.

## Experience in other countries

A submission for approval of gefitinib in NSCLC is currently before the Food and Drug Administration (FDA) in the US.<sup>11</sup> In September 2002, the FDA's Oncologic Drugs Advisory Committee recommended accelerated approval of gefitinib based on IDEAL 1 and IDEAL 2 study results. However, FDA reviewers were concerned that there was no non-gefitinib-treated control group, that there were a number of patients with slowly growing, less aggressive cancers that made evaluation of results complicated, and that there were a number of other confounding factors. This concern was reinforced with the release of the INTACT 1 and INTACT 2 study results, which showed no survival benefit with gefitinib when used as first-line therapy in combination with standard chemotherapy regimens.<sup>19</sup> It appears that the accelerated process has been put on hold and a decision from the FDA is not expected until May 2003.

Meanwhile, AstraZeneca announced in February 2003 that a Marketing Authorisation Application for gefitinib had been submitted in Europe for the treatment of locally advanced or metastatic NSCLC in patients who had failed prior chemotherapy.

Gefitinib has also been used for NSCLC in Western countries through expanded access programs, and has been trialled in patients with prostate, colorectal, breast, and head and neck cancers.<sup>1</sup>

## Risk factors

Various risk factors may contribute to the adverse reactions to gefitinib. Large interindividual variation in the metabolism of gefitinib may be one of the most important factors. But we believe another factor may be more important and this is related to the drug's mechanism of action.

Gefitinib inhibits the normal repair process when tissue is injured. Many patients received chemotherapy and/or radiation therapy before starting gefitinib and there may be residual tissue damage. Although this injury may be predictable, it is in precisely these patients that gefitinib has been used. In addition, infection may occur during the treatment course and the ensuing systemic inflammatory response syndrome may induce tissue injury in the lungs and various other organs. The process of repairing this injured lung tissue may be inhibited by gefitinib, with resulting pulmonary toxicity.

## Extensive promotion and wide use of unapproved gefitinib

Use of unapproved gefitinib commenced in December 2000, when it was provided free of charge on a compassionate basis. Brief product information was provided.

The price in Japan is now ¥7216 (approximately US\$60, €56 or £38) per 250 mg tablet, or more than ¥210 000 (approximately US\$1800) for one month's treatment at a dose of 250 mg daily.

AstraZeneca has several websites including their own, [www.astrazeneca.com](http://www.astrazeneca.com), a site specifically devoted to gefitinib (Iressa), [www.iressa.com](http://www.iressa.com), and one with information on EGFRs, [www.egfr-info.com](http://www.egfr-info.com), which includes a special journal, *Signal*. These sites can be accessed by patients and their families and appear to us to give a false expectation about the safety and efficacy of the drug.

## Conclusion

The regulation of information on websites is very difficult but premarketing promotion of unapproved drugs should be strictly controlled.

Expanded access programs, whereby new products are made available before approval on the grounds of compassionate use, are legal in the US and in European Union countries. However, it is very doubtful that prescribers and patients can access

sufficient information about unapproved drugs to make informed decisions about their use. Increased access to new products before approval is never ethical unless full information including animal toxicity studies and clinical trial results are disclosed. It is time to debate whether 'compassionate use' is ethical, even if full information is disclosed.

It is our opinion that the efficacy and safety of gefitinib and the regulatory approval process should be completely re-examined using data accumulated through clinical trials, expanded access programs and the postmarketing experience in Japan.

In the meantime gefitinib should be withdrawn, both in Japan and in Western countries where it is available through expanded access programs.

*Further information about gefitinib and the experience in Japan can be obtained from the authors.*

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# The pharmaceutical industry: power and profit

John Dowden, *Australian Prescriber* [jdowden@nps.org.au](mailto:jdowden@nps.org.au)

In November 2002 *The Lancet*<sup>1-4</sup> and the *BMJ*<sup>5</sup> published important articles about the influence of the pharmaceutical industry on medicine and society. The International Society of Drug Bulletins was well represented in these articles. Joe Collier of the *Drug and Therapeutics Bulletin (DTB)* was involved in planning and producing the series in *The Lancet* and, with Ike Iheanacho (also of *DTB*), wrote one of the articles. Danielle Bardelay and Christophe Kopp of *La Revue Prescrire* wrote a detailed commentary on the article in the *BMJ*.<sup>6</sup> Although the articles focused on the pharmaceutical industry in Western Europe and the USA, much of the information is relevant to other parts of the world.

## Drug regulation and information provision

One of the articles in the series in *The Lancet* discussed the powerful influence of the pharmaceutical industry on drug regulation.<sup>2</sup> The author of this article also wrote on the same subject for the *BMJ*.<sup>5</sup>

He argued that:

The more the pharmaceutical industry influences the perspective of the regulatory agency ... the more the agency could be said to be captured.<sup>2</sup>

'Regulatory capture' can occur in any country where the pharmaceutical industry funds the regulatory agency. To satisfy its paymaster the agency may be pressured into reducing the time it takes to evaluate a new drug. In 1989 the UK Medicines Control Agency took an average of 154 days to evaluate a new drug; in 1998 it took an average of only 44 days.<sup>2</sup> As an application to market a new drug may consist of hundreds of volumes of data, can we be sure that the agencies have enough time for stringent evaluation of the evidence?

We cannot assess the application data for ourselves because so much of it is kept secret. It is estimated that only half of the clinical trials included in an application are published within five years of a drug being licensed.<sup>1</sup> Often only the studies with positive results appear in medical journals. This causes a bias in the sum of the published evidence, which can cause difficulties for drug bulletins trying to write an accurate review of a drug.

Drug companies may argue that they provide all the information health professionals need to know when they market their drugs.

This information is contained in the labelling or the summary of product characteristics. In some countries the companies also produce information leaflets for patients. Although this information should be impartial, it may not tell people what they want to know. For example, it does not compare the product with other treatments for the same indication.

## Promotional activities and the pursuit of profit

The article in *The Lancet* by Joe Collier and Ike Iheanacho highlights the fact that drug companies spend far more on promotional activities than on provision of impartial information.<sup>1</sup> The impact of these activities can easily overwhelm the messages from independent drug bulletins. Because the promotion of drugs is so important, the marketing department of a drug company may even help design the protocols for clinical trials.

This market approach to drug development causes pharmaceutical companies to focus their research on drugs that will command high prices in developed countries. The pharmaceutical industry has mostly neglected developing countries, thereby failing a large proportion of the world's population.<sup>3</sup>

Although some companies have philanthropic programs to supply drugs to the developing world, these donations are not always helpful. Donated drugs may not be on a country's essential drug list and sometimes they are nearly out of date.

Perhaps there would be less need for donations if drug prices were not so high. Many developed countries subsidise the cost of drugs. This makes the drugs more

affordable for their own citizens, while maintaining the profits of the drug companies. However, it also ensures that many new drugs are beyond the reach of those in less developed countries.

The pursuit of profit is resulting in company mergers and cost cutting. One side effect of this corporate activity is that the companies may stop making useful but less profitable drugs. Companies that make generic products can help to maintain supplies and keep prices down, but this is often not possible for new drugs that are protected by patents for many years. Improved access to new drugs will require more liberal licensing agreements, but the pharmaceutical industry is more accountable to its shareholders than to society.

## Industry accountability

Making the pharmaceutical industry more accountable is difficult when the industry is wealthy and powerful. If the industry can capture regulatory agencies, it may also be able to influence governments. The industry can also use its influence indirectly through the institutions it funds. Even some consumer lobby groups are funded by the pharmaceutical industry.

The public interest may be served best by nongovernment organisations. The Medicines in Europe Forum, for example, has brought together several groups to campaign against any lowering of regulatory standards. This has helped to raise awareness in the European parliament that national governments are allowing their regulatory agencies to become servants of the pharmaceutical industry.<sup>6</sup>

## Industry viewpoint

The series of articles in *The Lancet* would have been complemented by a view from the pharmaceutical industry itself. The *BMJ* did include a commentary from a health economist who seemed to be a supporter of the pharmaceutical industry.<sup>7</sup> This economist argues that the ever more rapid release of new drugs is a good thing. The reduced evaluation time may reflect greater efficiency rather than regulatory agencies taking short cuts in their assessments.

## Summary

While there are benefits in making innovative drugs available, without long delays, to people who need them, very few new drugs are therapeutic advances. There seems little point in rapidly approving another ACE inhibitor or nonsteroidal anti-inflammatory drug, but this is what is happening.

As governments deregulate their economies there will be less control over the direction of research and the spread of information by the pharmaceutical industry. The balance of power is with the industry, not the regulators. It is therefore up to individual drug bulletins to inform health professionals and consumers about how safe and effective drugs are and to advise on the rational use of these drugs.

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## Coordinator's report

Andrea Tarr [andrea.tarr@which.co.uk](mailto:andrea.tarr@which.co.uk)

### Regional meetings

The committee hopes that at least one regional meeting will be organised in each ISDB region before the 2005 General Assembly. £2000 from ISDB funds will be available for each meeting. It is also likely that WHO will provide some assistance to cover expenses such as travel or accommodation.

For a meeting to be eligible for ISDB funding it must involve the active participation of at least 5 ISDB members, and at least 4 of these must be based in the region itself. Moreover, the organisers will need to provide an outline of the proposed meeting, which should include some assessment of the participants' views of the meeting as regards its content, perceived value, organisational arrangements, and so on. Once funding is agreed, the money would be guaranteed, with up to 25% paid in advance.

A meeting in Europe is already being planned for late 2003 in Berlin (see page 12).

The meeting for the Middle East and West Asia region, which was to be held later this year in Colombo, Sri Lanka, has been cancelled due to local difficulties.

### ISDB regions

AFRICA  
NORTH, SOUTH AND CENTRAL AMERICA  
EAST ASIA AND PACIFIC  
MIDDLE EAST AND WEST ASIA  
CENTRAL AND EASTERN EUROPE  
WESTERN EUROPE

### Committee and executive group meetings

An executive group meeting was held on 14 March 2003 in London. Minutes of this meeting will be included in the next issue of the newsletter.

A possible date for the next full committee meeting is the week of 15 September 2003.

### ISDB manual

In 1998 ISDB, in collaboration with WHO, began developing a manual on 'Starting or strengthening a drug bulletin'.

The aim of the manual was to document the knowledge of those involved in producing independent drug bulletins so that others could benefit from their experience.

All of the chapters had been written, and all except one had been circulated to reviewers and returned to the authors for revision, when work on the manual stopped in September 1999.

The new ISDB committee is determined that the project is completed, preferably this year. We know that WHO feels similarly and is prepared to help both technically and financially.

I have been contacting the authors to ask for their help in updating the chapters with the aim of finalising the text by mid-September 2003.

The committee hopes that the manual would then be published shortly afterwards (jointly with WHO) in print and electronic formats.

### Newsletter submissions

The deadline for submissions for inclusion in the next newsletter is 31 May 2003. Please forward submissions or enquiries to Mary Hemming at [mhemming@tg.com.au](mailto:mhemming@tg.com.au)

# ISDB Europe Regional Workshop

## Getting the most out of pharmacovigilance

<b>DATE</b>	<b>Friday 31 October and Saturday 1 November 2003</b>
<b>ORGANISERS</b>	<i>Arznei-Telegramm, Arzneimittelbrief, Pharma-Brief, Arzneiverordnung in der Praxis</i>
<b>LOCATION</b>	<i>Arznei-Telegramm Office, Bergstr. 38A (Water Tower), D-12169 BERLIN (Steglitz)</i>
<b>LANGUAGE</b>	<b>English</b>
<b>ISSUES TO BE ADDRESSED</b>	<i>What is the state of the art and how can it be improved? Which national systems are good examples to learn from? How can the generation of signals be improved? How can transparency of signal processing be improved? How can information on administrative handling of data be obtained? How can participation in the decision-making process be established? How can transparency of the decision-making process be ensured? What is the role of ISDB journals in drug safety evaluation? What does ISDB expect from national and European legislators? How can freedom of information be achieved and guaranteed?</i>

### DRAFT AGENDA

#### Friday 31 October

8.45 - 9.15	<b>REGISTRATION OF PARTICIPANTS</b>		<i>What can be achieved by pharmacovigilance centres? a) France b) Germany (Bremer Modell)</i>	16.00 - 16.30	<b>COFFEE BREAK</b>
9.15 - 9.30	<b>WELCOME ADDRESSES (ISDB President, host)</b>	12.45 - 13.15	<b>PLENARY DISCUSSION</b>	16.30 - 17.30	<b>WORKSHOP 4: What has to be improved? By whom? How?</b> <i>a) How to get information on and participation in decision-making b) How can the independence and quality of administrative decision-making be controlled and improved? c) How to deal with safety data in ISDB journals</i>
9.30 - 10.15	<b>INTRODUCTORY LECTURE: How can data on adverse drug reactions (ADRs) be obtained and what are the problems?</b> <i>What sort of data do we need? What are the best methods for obtaining data? What are the shortcomings and pitfalls of ADR monitoring and processing? How is an early discussion of new ADRs best organised?</i>	13.15 - 14.15	<b>LUNCH</b>		
		14.15 - 15.00	<b>INTRODUCTORY LECTURE: Effectively minimising drug risks and fostering drug safety by centralisation or decentralisation</b> <b>Does EMEA (the European Agency for the Evaluation of Medicinal Products) improve the detection of ADRs, data processing and decision-making in drug safety?</b>	17.30 - 18.00	<b>PLENARY DISCUSSION</b>
				Evening	<b>DOCUMENTATION</b> <i>Drafting of reports and resolution by rapporteurs</i>
10.15 - 11.15	<b>WORKSHOP 1: Spontaneous ADR monitoring system</b> <i>What can we learn from different countries regarding spontaneous reporting? a) UK b) Sweden</i>	15.00 - 16.00	<b>WORKSHOP 3: Data processing and decision-making in drug safety</b> <i>a) How does transparency and anti-transparency of EMEA and the drug industry influence risk management? b) How are the national scientific communities, national ADR monitoring committees or independent national experts integrated in processing safety data and decision-making?</i>		<b>Saturday 1 November</b>
11.15 - 11.45	<b>COFFEE BREAK</b>			9.00 - 11.30	<b>REPORTS</b> <i>Reports by rapporteurs Discussion of reports and draft resolution ISDB Europe resolution on pharmacovigilance</i>
11.45 - 12.45	<b>WORKSHOP 2: Systematic monitoring of ADR data</b> <i>What can we learn from different countries?</i>			11.30	<b>CLOSE AND FAREWELL</b>

*For more information, please email Wolfgang Becker-Brüser at [ati@berlin.snafu.de](mailto:ati@berlin.snafu.de)*

*If you would like to reserve a hotel room, please fill out the registration form on page 13*

# ISDB Europe Regional Workshop

## Getting the most out of pharmacovigilance

Friday 31 October and Saturday 1 November 2003

### HOTEL REGISTRATION FORM

We have booked rooms in a hotel a few bus stations away from the *Arznei-Telegramm* office  
(for passionate walkers it is within walking distance).

Single room per night: approx. €85

Please fill in this registration form and fax to (+49 30) 79 49 02 20

<b>I would like to make a reservation for</b>	
<b>Name</b> _____	
<b>Street</b> _____	
<b>Postcode</b>	<b>City</b>
_____	_____
<b>Country</b> _____	
<b>Bulletin/organisation</b> _____	
<b>Phone</b> _____	
<b>Fax</b> _____	
<b>Email</b> _____	
<input type="checkbox"/> ___ <b>Single room</b>	
<input type="checkbox"/> ___ <b>Double room</b>	
(check-in date)	(check-out date)
<b>From</b>	<b>To</b>
_____	_____
<b>Date</b>	<b>Signature</b>
_____	_____

# 2002 Financial Report

Andrea Tarr, ISDB Treasurer [andrea.tarr@which.co.uk](mailto:andrea.tarr@which.co.uk)

## Accounts 2002

### Income

Membership fees	£10 938
Donations from members	£1067
Bank interest	£31
<b>Total income</b>	<b>£12 036</b>

### Expenditure

Administration	
Website design and maintenance	£1545
Newsletter	£594
General Assembly (Dubrovnik)	
Venue hire and catering	£2103
Helping members with travel costs	£5384
Bank charges	£220
<b>Total expenditure</b>	<b>£9846</b>

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<b>Balance</b>	<b>£2190</b>
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<b>SURPLUS AT START OF 2002</b>	<b>£20 034</b>
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<b>SURPLUS AT START OF 2003</b>	<b>£22 224</b>
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## Draft budget 2003–2005

Estimated income	2003	2004	2005
Fees*	£10 300	£10 900	£10 900
Estimated expenditure	2003	2004	2005
Newsletter	£2700	£2700	£2700
Coordinator	£2770	£2770	£2770
Website	£500	£500	£500
Bank charges	£100	£100	£200
Regional meetings†	£4000	£4000	£2000
General Assembly	-	-	£10 000
<b>Total expenditure</b>	<b>£10 070</b>	<b>£10 070</b>	<b>£18 170</b>

### Summary

Most of the estimated income each year will be spent. In 2005, an excess of £7270 will be needed. If this is subtracted from the surplus available at the start of 2003 (£22 224), there will be £14 954 available for other activities (ie £4984 each year).

\* This estimate is based on the assumption that the number of members and the membership fee will remain the same as 2002. However, during the next 3 years there will be an attempt to increase full membership numbers and, if there is general agreement, the fees.

† The committee calculates that ISDB can afford to support 5 regional meetings during 2002-2005 (on average 2 per year). The amount for each meeting would be £2000.

## ISDB membership fees for 2003

Shortly you will receive an invoice for the ISDB membership fee for 2003, via either email or post.

The fee structure is the same as in previous years. There are three fee levels to ensure that there is no financial barrier to membership of the society, with suggested contributions depending on the overall budget of the bulletin or its parent organisation.

BUDGET	MEMBERSHIP FEE
£15–£5000	£5–£60
£5000–£20 000	£150
more than £20 000	£600

Recognised correspondents, as well as full members, are required to pay the fee. Please pay promptly. The ISDB constitution requires that the membership fee is paid no later than 2 months after receipt of the invoice.

# Minutes of the executive group meeting

16 December 2002, Drug and Therapeutics Bulletin Office, London

Prior to the meeting, a draft agenda was circulated to all members of the committee for comment. The final agenda, and discussion at the meeting itself, took these comments into account. After the meeting, draft minutes/proposals were sent to the committee and were subsequently approved.

Present: Joe Collier (president), Josef Tukker (secretary), Andrea Tarr (interim treasurer)

## 1) Executive group reports

### 1.1) The president

1.1.1) In September 2002, Joe Collier (with Josef Tukker and Andrea Tarr) produced a press release about the change in ISDB personnel following the elections at the General Assembly in Dubrovnik. The press release was taken up by the magazine *Scrip*, which published a brief report in October. Through an oversight the press release was not distributed to ISDB members until November.

1.1.2) During a pre-arranged trip to Australia and New Zealand, the president had the following meetings with ISDB members and other interested parties:

- On 7 November 2002 in Canberra, met with John Dowden and Craig Patterson (Australian Prescriber) and Mary Hemming (Therapeutic Guidelines).
- On 15 November 2002 in Wellington, met with Patricia Logan (PreMeC; National Preferred Medicines Centre), Peter Moodie and Tracy Barron (Pharmac), and Stewart Jessamine, Sarita Von Afelth and Karyn MacLennan (Medsafe).
- On 18 November 2002, visited a non-member publishing house (Best Practice Advocacy Centre) in Dunedin, talking with Chris Todd, Murray Tilyard and Tony Fraser.

1.1.3) The president had been in communication with Christophe Kopp (re succession arrangements), Darko Vrhovac (re review of the ISDB constitution), and Kathy Holloway (WHO Geneva; Daphne Fresle's replacement) and Kees de Joncheere (WHO Europe Regional Advisor on Pharmaceuticals and Technology) on relationships between ISDB and WHO.

### 1.2) The secretary

1.2.1) Since September 2002, Josef Tukker had reviewed the ISDB membership list. Inconsistencies and flaws were found in the current membership listing and an up-to-date and reliable list of full members and recognised correspondents was being constructed. It was envisaged that completion of the list would rely on a correspondence planned for the forthcoming newsletter. As soon as names and addresses were confirmed, they would be made available on the ISDB website.

### 1.3) The interim treasurer

1.3.1) Andrea Tarr had produced the 2002 Financial Report (see page 14), which included the following:

- accounts for the year 2002
- predicted positions for 2003, 2004 and 2005
- predicted costs for employing a coordinator and for producing three newsletters per year.

*(With the approval of the General Assembly, Andrea Tarr's work as treasurer had been undertaken on an interim, 3-month arrangement, until a full member of the committee could be identified who was prepared to fill the position. No such volunteer was forthcoming. After discussing the constitutional issues with Christophe Kopp, Joe Collier and Josef Tukker recommended to the committee that Andrea Tarr be coopted as a full member of the committee and that she continue to act as the definitive treasurer for this administration. This proposal was accepted.)*

## 2) Defining the specific tasks of the executive group and committee members

These were discussed and a draft set of duties/responsibilities was agreed as set out in Appendix 1 (see page 17). This was to be circulated to the committee for comment/ approval.

*(The duties/responsibilities were subsequently approved.)*

## 3) Defining the lines of communication between the executive group, the committee, and members

In keeping with the constitution, each year there will be three meetings of the executive group and one full meeting of the committee (possibly through video or audio link). Prior to a meeting of the executive group, a draft agenda will be sent to the full committee for comment. After a meeting of the executive group, draft minutes/proposals will be sent to the committee for comment/approval. The agreed minutes and proposals will then be published in the newsletter and/or website as appropriate.

## 4) Assessing ISDB's current and predicted financial situations

The current and predicted financial situations are provided in the 2002 Financial Report (see page 14). The report will be updated at the end of each calendar year. An official report will be submitted at the 2005 General Assembly.

## 5) Updating and overseeing the ISDB website

Maria Font had agreed to be webmaster. She will work with Josef Tukker and Andrea Tarr to keep the site up to date. Funds for this had been identified in the 2002 Financial Report (see page 14).

## 6) Maintaining and developing the ISDB newsletter

If invited, Mary Hemming would be willing to act as editor/producer (working with colleagues at Therapeutic Guidelines), with ISDB remaining as the publisher. The editor would commission articles and contributions and would be responsible for regular production and distribution. All material would be circulated for comment to the executive group before publishing.

The newsletter would have various dedicated sections with news and announcements from the president, secretary, coordinator, regional representatives, and others if and when appropriate. Other sections would be at the discretion of the editor.

The newsletter would have 3 issues per year. It would appear in electronic format and hardcopy. Those who specifically prefer to receive a hardcopy would notify the editor. The executive group accepted Mary Hemming's estimate that the cost of producing the newsletter along these lines would be £2700 per year.

*(Mary Hemming's appointment as editor of the newsletter was subsequently approved by the full committee.)*

## 7) Reports from the 2002 General Assembly and the voting on the constitution

Reports of the main outcomes of the 2002 Workshop and General Assembly in Dubrovnik will be set out in the newsletter. The result of the voting on the constitution will be dealt with in some detail. Possible ways of amending the voting system to make constitutional changes simpler will be explored by Darko Vrhovac.

## 8) Reviewing the position of the ISDB manual

It was agreed that Joe Collier would meet with Kathy Holloway (WHO Geneva) to seek ways of re-launching the ISDB manual project.

## 9) Planning future meetings

### 2005 General Assembly

It was decided that the date and venue for the 2005 General Assembly should be fixed by mid-2003. It was agreed that all members of ISDB should be invited to offer a bid. In the next issue of the newsletter an announcement will be made to this effect. Those bidding would need to give details of the location of the General Assembly, and its suitability. The information should include: estimated costs, venue services, suggested accommodation (including proximity to meeting venue), site accessibility (by air, car, train), and experience of the local staff in organising such meetings. The decision on the venue will be made by the full committee. It was stressed that ISDB is a worldwide organisation and that so far the majority of the meetings have been held in Europe.

### Regional meetings

The executive group calculated that ISDB can afford to support 5 regional meetings before the next General Assembly in 2005 (on average 2 per year). The amount provided for each meeting will be £2000. The executive group suggested that for a meeting to be eligible it must involve the active participation of at least 5 ISDB members, of which at least 4 must be based in the region itself. Moreover, the organisers would need to produce a proposal for the meeting with some assessment of the participants' views on its content, perceived value, organisational arrangements, etc. Once funding is agreed, the money would be guaranteed, with up to 25% paid in advance.

## 10) Brief review of priorities and actions for the next 3 years (ie until the next General Assembly in 2005)

The meetings listed in point 9 above were given a very high priority. The executive

group suggested that the 2005 General Assembly should probably last a little longer than it has in the past (say 5 to 6 days) and that the topics discussed should have a very wide appeal. The group suggested that the General Assembly should be seen as an occasion for developing ideas and producing solutions to ISDB problems worldwide.

In addition to the various meetings, the executive group considered that over the next 3 years there should be:

- a review/assessment of all member bulletins
- a program to continually update the website. All members should email Maria Font with any changes to do with their bulletin
- a strategy to strengthen links between the executive group, the committee, and bulletins locally. It is hoped that regional (local) coordinators will submit copy about local activity so that it can be published in the newsletter. Local coordinators will also be asked to identify possible new ISDB members and to contact Josef Tukker with their details. The executive group hopes that at least one regional meeting is organised for each region every 3 years
- a coordinator position (see projected ISDB expenditure in the 2002 Financial Report, page 14). Essentially he or she would: work for half a day per week; coordinate the executive group and internal communication; help organise regional meetings, where appropriate; coordinate special projects (eg the ISDB manual); and write reports in reply to requests from outside bodies. Joe Collier and Josef Tukker proposed that Andrea Tarr take on the role of ISDB coordinator.

*(This proposal was subsequently accepted by the full committee.)*

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## Appendix 1. Administrative tasks of executive group and committee members (2002-2005)

TASK	RESPONSIBILITY
Represent ISDB; oversee functioning and development; coordinate overall policy	President
Chair committee and executive group meetings	President
Approve budget reports	President
Compile newsletter (seek topics, liaise with authors, edit, coordinate, review/ proofreading, check format, layout, distribution, mailing, etc.); supply webmaster with PDF format if newsletter is to be included on website	Mary Hemming
Organise major meetings	President Secretary
Organise regional (local) meetings	President Secretary Regional (local) coordinator
Prepare annual budget and financial reports	Treasurer
Request payments of fees and follow-up letters to fee evaders	Treasurer
Ensure payments made, banking, etc.	Treasurer
Contact and encourage new applicants; applications for membership; collate responses; inform applicant; request payment of fee	Secretary
Maintain membership directory	Secretary
Draft agendas and minutes of executive group meetings	President Secretary
Webmaster	Maria Font
Review newsletter articles	All, as appropriate
Regional coordinators	To be decided

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