

Efforts to Improve Drug Information In Developing Countries

7

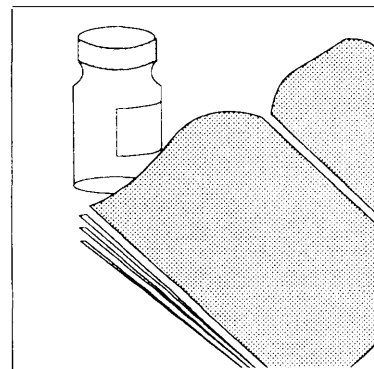
Drug labeling is not the only, or necessarily the most important, pharmaceutical issue facing developing countries, but it is recognized as an essential component of effective drug regulation. The World Health Organization (WHO), national governments, and private organizations have made efforts to promote the rational use of drugs, and within that broad objective, to improve the prescribing information available in developing countries. The activities of WHO, the U.S. Food and Drug Administration (FDA), and private groups related to drug labeling are discussed in this chapter.

THE WORLD HEALTH ORGANIZATION

In the past decade, pharmaceutical programs of the World Health Organization (WHO), in conjunction with other donors, have assisted developing countries in formulating comprehensive national drug policies (135). The focus of many national programs is pharmaceutical supply and consumption in the public sector, but strengthening regulation has been another priority. The following discussion covers briefly the main WHO activities directed specifically at improving drug regulation and prescribing information for physicians.

Action Program on Essential Drugs

WHO direct country support for pharmaceutical issues is provided primarily through the Action Program on Essential Drugs (APED). APED promotes the rational use of drugs all over the world, especially in developing countries. ¹The core of the



¹ For an overview of the history of the APED and the political constraints on WHO's efforts in this area, see reference number 183.

Action Program is WHO's "Model Essential Drug List," which can be adopted by countries, modified to fit their health needs, and used to promote the rational use of a limited number of pharmaceuticals. APED also promotes improved registration systems to better ensure that only safe, effective, and properly labeled products enter the market.

WHO provides training materials and seminars to achieve its goals. Among the publications relevant to drug labeling are: the *Model Guide to Good Prescribing* (286), developed in conjunction with the Groningen University in the Netherlands, and designed to be used in undergraduate medical education; the *Manual for Rural Health Workers: Diagnosis and Treatment with Essential Drugs* (47); and *The Essential Drugs Monitor*, a quarterly newspaper that discusses all aspects of essential drug programs, focusing on existing programs in developing countries. The *Essential Drugs Monitor* is distributed to 28,000 subscribers and is read by 180,000 people worldwide (286). APED also has a Documentation Center that distributes more than 20,000 publications a year and issues a periodically updated bibliography of available materials (on diskette and in printed form) (286).

Drug Management and Policies

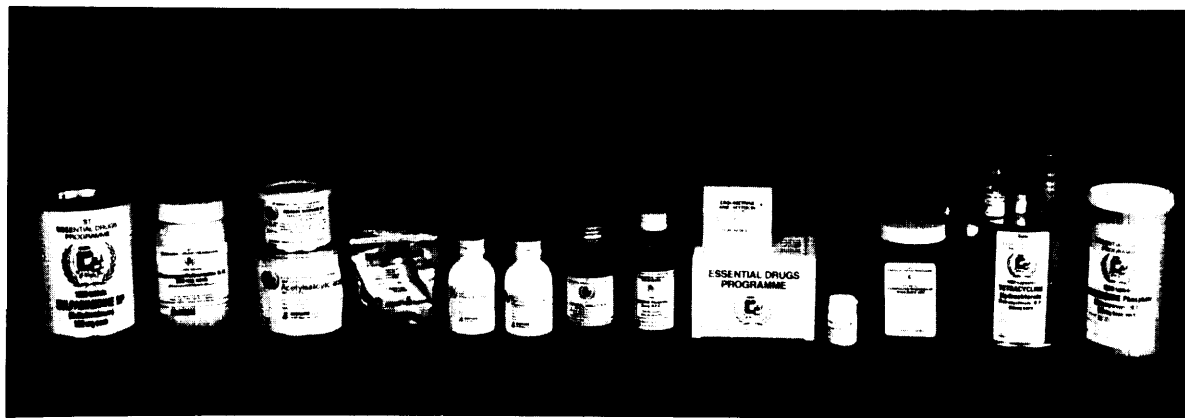
WHO's Division of Drug Management and Policies (DMP), which is independent of the

Action Programme on Essential Drugs, is responsible for a number of functions involving pharmaceutical issues. The DMP's units include Biological Standardization, Drug Regulatory Support, Drug Safety and Efficacy, and Quality Assurance. The DMP develops the *Model Prescribing Information* used by APED and coordinates the exchange of information on safety and efficacy of pharmaceuticals. In addition, the DMP is responsible for monitoring and further developing WHO's Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, which is discussed below.

WHO Certification Scheme

In 1969, WHO endorsed requirements for "Good Practices in the Manufacture and Quality Control of Drugs" (Guidelines on Good Manufacturing Standards) (285). These guidelines were the starting point for the "Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce," which was adopted in 1975 (275). The Certification Scheme was designed to assist countries lacking a comprehensive or effective drug control or registration system to ensure the safety and quality of imported drugs. Under the Certification Scheme, an importing country may request that the regulatory authority of the country in which the drug is manufactured provide a cer-

PHOTO CREDIT: T. FARKAS, WHO



Sample of WHO essential drugs.

tificate assuring that it was manufactured in accordance with good manufacturing practices. As originally designed, the certificate included the name and dosage form of the drug, the active ingredients, and either certified that the product was approved for marketing in the country of origin, or explained why it was not. In addition, the

PHOTO CREDIT: OXFAM PHOTO, WHO



Drug prescribing by village health worker in Bangladesh.

regulatory authority certified that the factory producing the drug was inspected regularly and complied with WHO guidelines on good manufacturing practices,

In 1984, the Third International Conference of Drug Regulatory Authorities (cosponsored by WHO and the U.S. FDA) recommended that the product labeling information approved in the country of origin be submitted with the certificate. They also recommended that the Certification Scheme be broadened to include imports of raw materials and unfinished products (275). These recommendations were adopted in 1988 (277). The new certificates require copies of all labeling supplied with the product in the country of origin, including approved packaging materials and package inserts (277).

WHO recently issued proposed new guidelines for the Certification Scheme, which were endorsed by the World Health Assembly (266). The new guidelines call for the issuance of one of

three different certificates: certificate of a pharmaceutical product (see figure 7-1), statement of licensing status of a pharmaceutical product, and batch certificate of a pharmaceutical product (285). The certificate of a pharmaceutical product is used by an importing country when: 1) the country is evaluating whether to approve a product for import and sale and 2) when administrative action is required to renew, extend, vary, or review an existing license for import and sale (285). The company exporting the product is responsible for requesting that a certificate be issued. So, if OTA, Inc. wished to export a drug to Thailand, and the Thai regulatory authority wanted a WHO certificate of a pharmaceutical product, OTA, Inc. would ask the FDA to issue a certificate to Thailand. Under WHO's Guidelines, the certificate is considered a confidential document.



PHOTO CREDIT: M. SENTIS, WHO

Man purchasing low-priced essential drugs in Nepal,

Figure 7-1—Facsimile of WHO Certification Program Certificate

Exporting (certifying) country: _____
 Importing (requesting) country: _____

Certificate of a Pharmaceutical Product

Proprietary name (if applicable) and dosage form: _____

Active ingredient(s) and amount(s) per unit dose: _____

1. Is this product licensed to be placed on the market for use in the exporting country? If yes, complete box A; if no, complete box B

<p>A</p> <p>Product licence holder: Status of licence holder: a <input type="checkbox"/> b <input type="checkbox"/> c <input type="checkbox"/> d <input type="checkbox"/></p> <p>Number of product licence and date of issue: is an approved technical summary appended? yes <input type="checkbox"/> no <input type="checkbox"/></p> <p>Is the attached product information complete and consonant with the licence? yes <input type="checkbox"/> non <input type="checkbox"/> not provided <input type="checkbox"/></p> <p>Applicant for certificate if different from the licence holder.</p>	<p>B</p> <p>Applicant for certificate: status of applicant: a <input type="checkbox"/> b <input type="checkbox"/> c <input type="checkbox"/> d <input type="checkbox"/></p> <p>Why is authorization lacking?: not <input type="checkbox"/> not <input type="checkbox"/> under <input type="checkbox"/> refused required required consideration</p> <p>Remarks:</p>
--	--

2. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced?
 yes no If No, proceed to question 3

Periodicity of routine inspections (years): _____

Has the manufacture of this type of dosage form been inspected? yes no

Do the facilities and operations conform to GMP as recommended by the World Health Organization? yes no

3. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party?
 yes no If no, explain: _____

Address of certifying authority: _____	Name of authorized person: _____
	Signature: _____
	Stamp and date: _____

Telephone/fax numbers: _____

This certificate conforms to the format recommended by the World Health Organization.

● Specify whether the person responsible for placing the product on the market;

- manufactures the active ingredients and the finished dosage form;
- manufactures the finished dosage form;
- packages and/or labels a finished dosage form manufactured by an independent company;
- is involved in none of the above.

SOURCE: World Health Organization, *Implementation of WHO's Revised Drug Strategy-Safety and Efficacy of Pharmaceutical Products, Progress Report of the Director General, A45/13* (Geneva, Switzerland: WHO, 1992).

The statement of licensing status of a product attests that the product has been licensed for sale in the country of export. The statement is intended to be used by importers considering bids made in response to an international tender for drugs (285). The batch certificate of a pharmaceutical product provides information on the quality and expiration date of a specific batch of the product, including results of any analyses undertaken on the batch. For most products, the batch certificate is issued by the manufacturer. For vaccines, sera, and other biological products, the certificate is issued by the regulatory authority (285).

By 1990, 129 countries had notified WHO that they intended to use the Certification Scheme; however, most of the countries opted to use it as a means of controlling imports, not as a means to support exports (52). Countries were regularly requesting certificates for imports, but did not have a policy of providing certificates with exports. This is not surprising because in order to issue a certificate a country must ensure that:

- the authorization for sale or distribution is subject to appropriate testing,
- its pharmaceutical industry conforms with recommended standards for the manufacture and quality control of pharmaceuticals,
- the competent authority is given the authority to carry out complete inspections of the pharmaceutical manufacturing facilities, and
- the country's inspectors are qualified and experienced.

It is likely that only those countries with developed drug regulatory bodies could provide certificates that meet these criteria (285). In addition, evidence suggests that the Scheme is not used optimally by developing countries, particularly in Africa, which relies heavily on imported pharmaceuticals (275,200).

The Certification Scheme has limitations. Certificates may be difficult to obtain for drugs manufactured in more than one country or manufactured in one country and packaged in another.

Donated drugs or drugs procured from wholesalers and brokers with a wide variety of sources may not be easily certified. Products manufactured specifically for a foreign agency or government may differ from the manufacturer's standard products and labeling from the standard product may not be appropriate for the special product (275). If a country requests a certificate only at the time of first import or when a drug is reregistered, the country may not obtain updated



PHOTO CREDIT: P. MERQUEZ/WHO

Transport of essential drugs in Latin America

information about the drug (164). Countries with inadequate administrative or legal infrastructure for drug regulation may be unable to use the Certification Scheme effectively (164).

APED and DMP have initiated activities to improve the Certification Scheme and expand its adoption. The United States Agency for International Development (USAID) is supporting a WHO evaluation of the Certification Scheme in

developing countries and the DMP is carrying out field trials in a number of countries (259, 286).

Distribution of Prescribing Information

In addition to labeling provided with a drug, compendia of pharmaceutical information from industrialized countries are useful sources of prescribing information for officials and physicians. WHO is working to provide national drug regulatory authorities in developing countries with three of these compendia, which contain information approved by the regulatory authorities in those countries: the *Dictionnaire Vidal* (249) (information approved by the French Ministry of Health); Association of the British Pharmaceutical Industry *Data Sheet Compendium* (10) (information in compliance with the regulations of the United Kingdom), and the *Physicians' Desk Reference* (information in compliance with regulations of the U.S. FDA) (258).

DMP has also begun work on a series of publications entitled *WHO Model Prescribing Information* for those drugs on the essential drugs list that are of particular interest to developing countries. The first one, *Drugs Used in Anesthesia* (280), was published in 1989; *Drugs Used in Parasitic Diseases* (282) was released during 1990; and *Drugs Used in Mycobacterial Diseases* (284) in 1991, with more in preparation.²

Access to New Information on Safety and Efficacy of Pharmaceuticals

Most industrialized countries have formal programs for monitoring adverse reactions associated with pharmaceuticals. Developing countries typically do not have the resources to do this in their own countries, and as a result, may not be able to respond to the need to revise labeling, or

even withdraw a drug from the market. One WHO priority is to secure the regular exchange of information on the safety and efficacy of pharmaceuticals and to promptly transmit new information on serious side effects to national health authorities (258). The DMP receives information regularly on decisions of regulatory authorities and voluntary decisions of manufacturers related to the safety of pharmaceuticals. During 1986, for example, WHO received information on decisions about 360 pharmaceutical products from 35 countries (258). This information is disseminated monthly to the drug regulatory authorities of member countries through the *WHO Pharmaceutical Newsletter* (285). DMP also produces *WHO Drug Information*, a quarterly journal that provides discursive commentaries on the more important actions of national drug regulatory bodies (258,285).

WHO has established collaborating centers in each of its five regions for the purpose of information dissemination, training, and operational research. The most recent collaborating center was established in India in 1988 to serve 11 countries in Southeast Asia (131,274).

These collaborating centers are distinct from the WHO Collaborating Centre for International Drug Monitoring in Uppsala, Sweden, which is an international center for monitoring adverse drug reactions. Thirty-three countries, including the United States, provide case reports on adverse drug reactions to the Uppsala Centre where the data are combined and analyzed to detect relationships between drugs and rare adverse reactions (290). The information in the database at Uppsala, which as of 1991 contained 950,000 individual case reports (290), is available only to the countries that participate in reporting. Nonparticipating countries may learn about the adverse reactions through medical journals or through the regulatory actions of participating

² WHO is currently working on prescribing guides for drugs used in treating sexually transmitted diseases, including AIDS, and other bacterial diseases, and in neurology and dermatology (285).

countries, but there is no guarantee that they, in fact, will (290).

THE U.S. FOOD AND DRUG ADMINISTRATION

The FDA is primarily a domestic agency, but being the regulatory agency for one of the largest pharmaceutical markets in the world, it is also involved in international pharmaceutical issues. The FDA is not a development agency and it does not generally help other countries with projects specifically designed to improve the marketing and labeling of drugs, but it does assist developing countries by sharing its expertise with their drug regulatory personnel.

Most of FDA's international activities are coordinated by its International Affairs Staff (IAS) under the Associate Commissioner for Health Affairs. The IAS is principal FDA contact point and liaison with foreign counterpart agencies, foreign embassies, international regional organizations, U.S. Government agencies (e. g., the Office of International Affairs, U.S. Public Health Service; USAID, the U.S. Trade Representative), and U.S. embassies. IAS arranges the participation of FDA officials in U.S. delegations to international meetings, such as those held by WHO. Four IAS officials are responsible for bilateral liaison within broad geographic regions.

One of FDA's most visible international activities is the dissemination of information about regulatory actions. FDA sends monthly updates to WHO and representatives of the European Community on important regulatory developments, including proposed regulations and policies; reports of serious adverse reactions from pharmaceuticals; the monthly list of approvals for new drugs, medical devices, and biologics; and other public information. WHO may incorporate this information in its newsletters, which are distributed internationally.

The FDA also sends its *Medical Bulletin* (see, e.g., ref. 150) to more than 800 government and academic organizations around the world. Many

of these institutions are in industrialized countries (e.g., more than 129 Canadian institutions are on FDA's mailing list), but a number are in developing countries. The *Medical Bulletin* focuses on new FDA policies and findings on particular drugs and devices. For example, a recent issue discussed the dangers of angiotensin converting enzyme (ACE) inhibitors during the second and third trimesters of pregnancy, allergic reactions with dialysis and ACE inhibitors, new Halcion labeling, warnings about sporicidin products, FDA proposed food labeling reforms, recommendations on silicone breast implants, and foodborne diseases in nursing homes (150).

Until the end of 1991, the FDA sent quarterly information packets to WHO, the Pan American Health Organization (PAHO), and approximately 70 drug regulatory authorities throughout the world (95). This policy has now modified to sending important policy papers to WHO and to 62 foreign embassies located in Washington, DC. The material sent by FDA does not necessarily focus on labeling for specific drugs but instead highlights regulatory decisions that U.S. regulators believe are important (32).

The FDA also has a special procedure for notifying foreign purchasers that a drug or medical device has been withdrawn from the U.S. market for safety reasons. FDA contacts the U.S. company for a list of foreign individuals, institutions, and government agencies that have imported the product. The IAS works with the U.S. Department of State to provide the U.S. embassies in the countries in which the product is sold with a list of the purchasers so that the purchasers can be notified (168). FDA provides a summary of the reasons for withdrawal, and encourages the U.S. company to provide foreign purchasers with complete information. FDA may evaluate the effectiveness of the company's notice by requesting that the U.S. embassies follow up with foreign purchasers to see whether information was provided. If the company has not provided adequate information, FDA may ask them to send it but does so without legal authority. There have

been few drug withdrawals in which FDA has used this special notification procedure (31).

FDA also responds to requests for information from other countries. FDA is currently setting up an electronic bulletin board that will contain all public information issued by the FDA including: *Enforcement Report* (weekly recall list), a drug and device product approval list, *Medical Devices and Radiological Health* news, *FDA Medical Bulletin*, *FDA Consumer Information*, FDA's *Federal Register* summaries, speeches by FDA officials, FDA congressional testimony, special AIDS information, *Veterinary Medicine* news, and notice of upcoming FDA public meetings. The electronic information will be available through INTERNET, a worldwide research computer network of government, military, academic, and other organizations (32).

The IAS administers the FDA International Visitors Program. In the year ending September 1991, FDA was visited by 603 representatives from 61 countries. In 1990, the IAS arranged visits to the FDA by 789 foreign officials representing 65 countries and multinational organizations (168).

FDA cooperates with WHO in various activities. In 1980, the FDA and WHO cosponsored the first International Conference of Drug Regulatory Authorities, held biannually since then, bringing together regulatory authorities from all over the world. FDA representatives have provided advice and other assistance to various WHO programs including the Action Program on Essential Drugs, WHO's Management Advisory Committee, the Certification Scheme, the Ethical Criteria for Medicinal Drug Promotion, the preparation of Model Drug Prescribing Information, the Model Lists of Essential Drugs, and the Global Program on AIDS (166). FDA is also a WHO Collaborating Center for Monitoring of

Adverse Drug Reactions, providing WHO with a monthly accounting of all serious adverse reaction reports (168).

FDA staff have also assisted WHO with drug regulation projects in developing countries (17). In 1988, for example, the FDA provided a drug specialist for 2 years to PAHO, a regional office of WHO, to assist with formal training programs designed to strengthen national drug agencies and improve pharmaceutical manufacturing (57). Most recently, the FDA agreed to assist USAID in its support of a WHO evaluation of the Certification Scheme (see above) (24,259), and USAID and the FDA will assist in a WHO evaluation of its "Guiding Principles for Small National Authorities" (24, 278).

THE U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT

Until recently, USAID was not involved directly with WHO's pharmaceutical work, but has just begun funding a WHO evaluation of both the Certification Scheme and the "Guiding Principles for Small National Authorities." USAID is also supporting a WHO project to develop country-specific research on current pharmaceutical use in developing countries. The research will be carried out by the International Network for the Rational Use of Drugs (INRUD) (see below for description of INRUD), which will develop a *Drug Use Indicators Manual*. The manual will include background, definitions, methodologies for collecting drug use indicators,³ and extensive appendices containing data collection methods, drug and problem lists, and data collection forms (24,113). A report on these activities should be available by the end of 1992.

USAID is also engaged in a 5-year cooperative agreement with the U.S. Pharmacopoeia to assess and facilitate the distribution of pharmaceutical

³ Drug use indicators include: average number of drugs used per facility; percent of antibiotics or injections; percent of patients not provided drugs; number of essential drugs in stock, patients reporting correct dosing, etc. (1 13).

information in developing countries, including both information provided to the drug regulatory authorities and to health workers (24). Finally, US AID has requested proposals for a 5-year contract addressing three areas of pharmaceutical distribution in developing countries: drug regulation and registration; rationalization of procurement strategies; and the development of pharmaceutical information for prescribers, consumers, and drug regulatory authorities (24).

CONSUMER HEALTH ADVOCATES

A variety of organizations and individuals address themselves to pharmaceutical issues in developing countries. This section concentrates on groups that act as advocates for political change or focus on the role of multinational pharmaceutical companies in the area of drug information. The many organizations that provide health care or focus on health issues other than pharmaceuticals are not discussed here.

Public health advocacy may take several forms. The most common form is the dissemination of information to the public and the press about actions of industry, international organizations, or governments, that are inconsistent with consumer interests. Consumer boycotts, while difficult to organize, can also be powerful. In addition, public interest organizations may operate as information clearinghouses and many provide educational programs in developing countries.

Numerous public interest groups operate in individual countries. Many of the individual health and consumer groups in both developing and industrialized countries are part of a larger international network, Health Action International (HAI), which itself works closely with the International Organization of Consumers Unions, an umbrella group that helps promote consumer issues and consumer advocacy in many countries. These two groups and selected smaller consumer groups are discussed below.

The International Organization of Consumers Unions

The International Organization of Consumers Unions (IOCU) was formed in 1960 as a multi-purpose resource for its membership of 130 consumer groups in 51 countries. IOCU's central office is in the Hague, and its two regional offices are in Penang, Malaysia, and Santiago, Chile. IOCU acts as an information network, coordinates consumer activities, holds a triannual world congress, and organizes international seminars and workshops. In 1973, IOCU published one of the first studies on drug labeling in developing countries (see app. A) (61,116) and it continues to be active in drug information as well as other issues of pharmaceutical distribution. In August 1990, IOCU sponsored an International Workshop on Consumer Health and Drug Information and Education in Penang, Malaysia. The major objective of the workshop was to determine how media could be used effectively to communicate information to parents about children's health and the rational use of drugs (54).

IOCU drug labeling activities include collecting relevant information (e.g., general prescribing information, lists of banned or restricted pharmaceuticals, reports of adverse effects) and passing this information on to developing countries. IOCU also publishes reports related to the pharmaceutical industry and rational drug use. In 1981, IOCU published a *Consumer Action and Resource Kit on Pharmaceuticals*, which focused on 44 "problem" drugs, that could be used by groups in developing countries to lobby against the sale of dangerous drugs (154).

IOCU also maintains a network called Consumer Interpol, consisting of approximately 260 correspondents in 79 developing and developed *countries* (117). The correspondents monitor information on newly discovered or newly regulated hazardous consumer products, including pharmaceuticals, such as notifications of banning, restriction, withdrawal, or nonapproval of products. This information is received by the Con-

sumer Interpol office in Penang and may become the basis for *Consumer Alerts* sent to all members of the network. As of March 1991, 85 *Consumer Alerts* had been sent out, covering hazardous toys, cosmetics, pharmaceuticals, electrical goods, food products, pesticides, and other items (4). Consumer Interpol also distributes a *Consumer Interpol Memo*, relating selected articles and news briefs on consumer issues, and a quarterly *Consumer Interpol Focus*, with feature stories on specific safety problems or major international initiatives to restrict global trade in hazardous products (3).

IOCU has published many books and pamphlets on technical aspects of pharmaceutical use. In 1988 it published several short pamphlets written by its pharmaceutical adviser, K. Balasubramaniam, including: *Policy Options in Pharmaceutical Patents for Developing Asian Countries* (14); *The Rational Use of Drugs: A Universal Concept* (15); *Global Marketing of Pharmaceuticals: Prescription for Disaster* (12); and *Policies and Strategies On Drug Pricing Regulations: International Experiences* (13). IOCU also supports publications by other consumer organizations.

With respect to pharmaceutical issues, IOCU plays a major role in one of the primary international consumer health organizations, Health Action International.

Health Action International

In 1981, 50 consumer organizations and individuals founded Health Action International (HAI) as an “international antibody” to the adverse effects of pharmaceutical marketing. HAI has coordinating offices in Europe, Asia, and Latin America. HAI’s original agenda included (102):

1. developing an information clearinghouse;
2. responding to the IFPMA Code of Pharmaceutical Marketing Practices;
3. coordinating activist campaigns regarding specific drugs and companies;

4. promoting full implementation of WHO’s Action program on Essential Drugs;
5. pressuring industry to market drugs that meet “real medical needs,” have “significant medical value,” and are acceptably safe and efficacious; and
6. supporting nondrug solutions to health problems.

HAI has coordinated international advocacy for essential drug policies in lobbying WHO, UNICEF, the European Parliament, and other international and regional bodies (16,97).

For a number of years, HAI lobbied WHO to pass a code of pharmaceutical marketing. In 1982, HAI published its own code of conduct that it hoped would be the basis for a U.N. or WHO international code. The HAI code demonstrates the degree of specificity that consumer groups seek. With respect to labeling, HAI’s code calls for package labels with:

1. specific information on whether the product is for prescription or OTC use;
2. the non-proprietary name for all active ingredients printed in equal or greater size than the print used for the manufacturer’s name;
3. information on the class and category of therapeutic use;
4. an explanation of all contraindications that may endanger life or severely endanger health; and
5. a list of all active ingredients.

HAI also would limit claims about efficacy, safety, or potency of the product unless they were qualified. In addition, the HAI Code would require that package inserts include: 1) only those indications approved by public health authorities or generally endorsed by reputable and independent scientific publications, 2) all contraindications that are not included on package label, and 3) a list of active and inactive ingredients (84). Finally, HAI would require graphic warning symbols on all promotional material indicating

products that should be avoided during pregnancy or lactation, on all prescription-only products to indicate changes in product information, and on new products for which reports of any adverse reactions or events are required (86).

HAI has published a detailed critique of the IFPMA Code and WHO's Ethical Criteria for Medicinal Drug Promotion (see ch. 6) (86). Another report by HAI presents evidence that the IFPMA Code is not effective in controlling advertising (39). In 1992, HAI carried out the first phase of an international survey of pharmaceutical marketing standards that will evaluate the implementation of WHO's Ethical Criteria for Medicinal Drug Promotion (97). Initial results indicate that the Ethical Criteria have not been effective because they have not been implemented at the national level (89).

HAI member groups also focus on problems with specific products or categories of product, trying either to have the products removed from the market or to change their labeling or promotion. Their campaigns usually consist of documenting problems with drug products, challenging the companies involved to respond to their criticisms and, if the company responses are not satisfactory, using public education campaigns "built on solid information and powerful emotional pleas" (102). The organization communicates through an international newsletter, *HAI News*.

One HAI international campaign was directed at removing inappropriate antidiarrheals from the market. Following a WHO paper on the limited efficacy of antidiarrhea drugs, HAI members in Latin America published a survey of antidiarrhea drugs marketed in Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Guatemala, Mexico, Peru, Uruguay, and Venezuela. A number of products that WHO said were not efficacious, and potentially harmful, were widely available in those countries (87).

HAI has published various resource books on pharmaceuticals. *Problem Drugs* (38), a HAI "information and campaign pack" on various cate-

gories of "problem" pharmaceuticals, was first published in 1986. It has since been translated into 8 languages and a new edition is scheduled for release in 1993 (97). Other publications include: *Peddling Placebos: An Analysis of Cough and Cold Remedies* (36), *Antibiotics: The Wrong Drugs for Diarrhoea* (35), *Cleared for Export* (33), *The Provision and Use of Drugs in Developing Countries* (71), *Drugs and Primary Health Care* (63), *Promoting Health or Pushing Drugs? A Critical Examination of Marketing of Pharmaceuticals* (39), *A Question of Control* (261), and *Bitter Facts About Drugs* (5). Andrew Chetley, a prominent consumer advocate who has worked with a number of consumer groups, is the author of several of these publications and has recently written a book analyzing the role the pharmaceutical industry has played in health care in the developing world (37).

In addition to its publications and lobbying, HAI groups help promote and develop national drug policies and sponsor a wide variety of training and education programs. HAI seeks to promote the WHO Ethical Criteria for Medicinal Drug Promotion, and continues to expand and strengthen its ties to local consumer organizations in developing countries (88).

SOCIAL AUDIT

Social Audit, based in the United Kingdom, is an active HAI member. It has concentrated on the marketing practices of British multinational pharmaceutical corporations in developing countries, but it also has examined their activities in industrialized countries. In 1979, Social Audit published *Insult or Injury? An Enquiry into the Marketing and Advertising of British Food and Drug Products in the Third World* (142), a work funded largely by IOCU. In 1982, the group published *Drug Diplomacy: Decoding the Conduct of a Multinational Pharmaceutical Company* (148). This book chronicles Social Audit's campaign against the marketing claims made by Searle Pharmaceuticals for its antidiarrhea drug

Lomotil, a campaign that Social Audit maintains resulted in changes in the labeling (154).

In 1980, Social Audit published *Drug Disinformation: What British and Multinational Drug Companies Tell Doctors About Their Products, At Home and Abroad* (143). This book compared the information for about 900 drugs listed in MIMS prescribing guides in England and Ireland. Although over half of the entries were identical, the study found what they believed to be significant discrepancies for the prescribing entries for over 200 products.

The main force behind Social Audit is its Director, Charles Medawar. He continues to publish books and articles that keep the work of Social Audit visible. In addition to the titles listed above, he has written: *The Wrong Kind of Medicine?* (144), *Drugs and World Health* (146), “International Regulation of the Supply and Use of Pharmaceuticals” (145), and with the support of IOCU, *One Drug at A Time: A Report on the Limitation of Fixed Ratio Combination Drugs* (149). In 1991, Social Audit published *Power and Dependence* (147), an examination of the history of benzodiazepine (a class of sedatives that includes diazepam) marketing, focusing on the problems of dependence.

BUKO

BUKO (the Federal Congress of Development Action Groups), one of the founding members of HAI, is a West German network of approximately 200 consumer groups that focuses on “global malpractice in drug marketing by the multinational pharmaceutical companies” (62), in particular Swiss and German companies. In 1987, it published a short report on Hoechst, a German pharmaceutical company, with evidence that Hoechst was marketing drugs in developing countries that had potentially severe side effects, or which had been banned in developed countries, often without complete warnings (62). The study also attacked Hoechst’s practices in Germany, such as the delay of a **warnin g** letter to German doctors about several reported adverse

reactions (including six deaths) caused by one of its antidepressant products (62).

In 1990, BUKO, together with HAI, helped disseminate a study by two German physicians that examined more than 2,000 German and Swiss pharmaceutical products marketed in 26 developing countries. The majority of these products were marketed by large multinational corporations. The authors determined whether these drugs met the health needs of the countries in which they were marketed by comparing the sample drugs to those on WHO’s Essential Drug List. The authors also evaluated the efficacy and safety of the drugs using authoritative pharmaceutical reference books from several countries (7,28,30,75). They reported significant problems in all areas. (See app. A, “The Hartog and Schulte-Sasse Study.”)

In addition to its publications, BUKO produces a monthly newsletter *Pharma-Brief*. The newsletter contains summaries of research on pharmaceutical issues in developing countries and reports on consumer activities (64). BUKO also helps facilitate dialogue on pharmaceutical policies in developing countries. In 1987, for example, BUKO held a conference in Germany that brought together representatives of nongovernmental organizations from various developing countries, academia, and industry. The conference focused on the relationship among the number of pharmaceuticals on the market in a country, the quality of those products, and the need for essential drug policies in countries with limited budgets for health care (85).

Medical Lobby for Appropriate Marketing (MaLAM)

MaLAM is an international network of physicians that acts as a watchdog for advertising by pharmaceutical companies (199). MaLAM works to encourage companies to provide what they consider “sufficient, consistent, and accurate information” about their products, and primarily

targets marketing claims made in developing countries (254).

Each month, MaLAM's approximately 700 subscribers in more than 40 countries receive a draft letter addressed to a senior executive in a pharmaceutical company questioning a particular marketing practice. MaLAM subscribers are asked to sign the letter and return it to MaLAM. A final letter is sent after review by an international editorial board (153,254). The letters ask the company to provide evidence supporting the contested advertising claim. MaLAM publishes the responses it receives from industry in its newsletter. (Results of some of MaLAM's work are discussed in ch. 4 and 6.)

International Network for the Rational Use of Drugs (INRUD)

Developing countries typically lack the resources needed to evaluate national programs, including drug policies. An organization that provides support for evaluative research is the International Network for the Rational Use of Drugs (INRUD), a nonprofit group based in Boston. INRUD is a cooperative organization of health professionals, administrators, and researchers from developing countries who are interested in implementing new, innovative programs to improve the use of pharmaceuticals, and is supported by the development agencies of a number of countries (including USAID) and private foundations (127).

INRUD's strategy is to first engage in research designed to clarify the "dynamics of drug use and . . . the underlying motivations, expectations, and incentives of providers and consumers" (128). According to INRUD, *although a number of countries have tried to improve drug use by developing standard treatment protocols, providing drug information, drug bulletins, implementing changes in health training curricula, restricting drug advertising, and using public education, there has been little evaluation of these strategies; they are assumed to have a positive impact.*

However, studies in industrialized countries have revealed that some of these same interventions have not been very effective (127).

The initial INRUD network is limited to seven countries that have demonstrated a commitment to the rational use of essential drugs: Bangladesh, Ghana, Nigeria, the Sudan, Tanzania, Indonesia, and Nepal. Each country has a "Country Core Group" of four to eight people representing various professional disciplines and organizations. A "Central Support Group" is staffed by Management Sciences for Health and the Harvard Medical School in Boston. INRUD anticipates that other individuals and organizations interested in the program will become affiliate members and share in information gathering, training, and other activities (128).

INRUD also is developing a number of indicators of drug use to facilitate comparisons of drug use among countries and identify drug use problems. The study involves field work in Indonesia, Bangladesh, Nepal, Nigeria, and Tanzania. WHO plans to publish a manual on standard drug use indicators based on the results of this study (115). INRUD recently received a grant from US AID to conduct country-specific research with WHO on current pharmaceutical use in developing countries (see section on USAID, above).

INRUD publishes a newsletter, *INRUD NEWS*, reporting on its own activities and on other recent drug utilization studies, and has developed a computerized bibliography of published and unpublished literature relating to drug use in developing countries (114). In addition, INRUD has developed training materials to promote rational drug use, which it has used in Nepal and will use in Zimbabwe in 1993. INRUD's future plans include studies of the factors that influence drug prescribing behavior (129).

SUMMARY

Developing countries face many obstacles to maintaining effective pharmaceutical programs,

154 | Drug Labeling in Developing Countries

including lack of political commitment, poor planning capabilities, lack of trained personnel, inadequate financial resources, irrational prescribing and dispensing practices, and lack of public awareness of the problems (286). WHO

programs and private groups have attempted to help countries by providing information and other services to improve drug regulation, including the regulation of drug labeling.