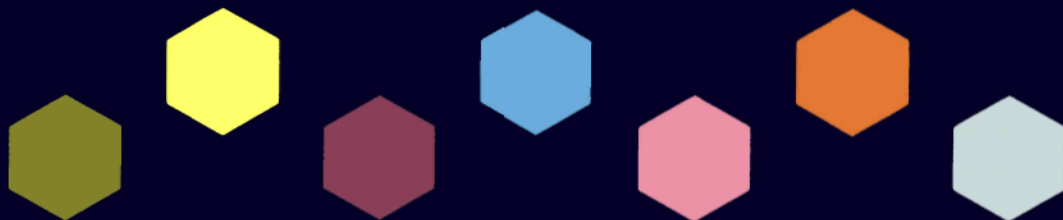

WHO DRUG



INFORMATION

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PROPOSED INN LIST 76
INTERNATIONAL NONPROPRIETARY NAMES
FOR PHARMACEUTICAL SUBSTANCES



WORLD HEALTH ORGANIZATION · GENEVA

WHO Drug Information

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General Policy Topics

Meeting the challenge of biotechnology

It is acknowledged that biological substances used in the practice of medicine make a vital contribution to public health. Nevertheless, because of their very nature, biologicals demand special attention with regard to their regulation and quality control.

Biologicals, which include vaccines and blood products, cannot be completely defined by physico-chemical criteria alone and often require a biological assay to guarantee potency. The considerable potential hazard associated with some of these substances requires that continuous vigilance and control must be exercised.

By definition, these substances are derived by biological processes which are known to be inherently variable, a feature that has important consequences for the safety and efficacy of the resulting product. A prerequisite for the use of biologicals is therefore to assure the consistency of quality and safety from lot to lot. For this purpose, in-process laboratory-based controls must be in place.

Today, the biologicals field is one of enormous expansion and increasing diversity, most especially in the area of new biotechnologies. The revolution in DNA-based and other cell technologies has opened up a new and exciting vista for global health care and, in many instances, traditional products are being replaced by equivalents derived by recombinant DNA technology.

New possibilities for diagnostic procedures are also emerging, such as the use of nucleic acid (gene) amplification methods for the virological safety testing of blood and blood products. Nucleic acid amplification techniques involving the polymerase chain reaction (PCR) have exceptional sensitivity and specificity for the detection of viral nucleic acids. Their use for improving the reliability of testing to ensure the virological safety of blood and blood products will have considerable public health benefits.

There are also exciting new approaches to improved vaccination through the use of DNA-

vaccines. The discovery in 1990 that the injection of plasmid DNA into mouse muscle resulted in the expression of encoded genes *in vivo* led to the prospect of using DNA itself as vaccine material. Its injection into muscle results in long-term expression of an encoded antigen together with the development of appropriate immune responses and host protection. Much research and development work is still needed, but many potential benefits to public health can be envisaged.

Unlike traditional biologicals, many of these new products are extremely pure and highly characterized. Nevertheless, great care must be taken regarding their safety and quality because of the novel processes used in their manufacture and the complex structural and biological characteristics of the products themselves. There is also a need to be absolutely sure that consistent and reliable results are obtained by industry and public health laboratories when applying the new nucleic acid amplification techniques.

New biotechnology-based products, such as vaccines and diagnostics, need to be appropriately incorporated into the health care systems of all countries, and mechanisms need to be in place to ensure that these products are made available to all who need them. Although the development of gene therapy and DNA-vaccines has taken place primarily in developed countries, biotechnology is evolving rapidly in an increasing number of developing countries. Since decisions will need to be made on the regulation and testing of these new products and procedures, it is important that respected worldwide standards of quality and safety are in place. Adequate control measures are essential, both to safeguard recipients of these products against adverse effects, and to ensure that the full benefits of scientific innovation are available to all.

The early availability of guidelines on the production and quality control of biotechnology-derived medicinal products in Europe and the United States, for example, has been particularly instrumental in establishing the quality, safety and efficacy of recombinant DNA-derived products in those regions. Such guidelines provide the basis for a well-balanced, sound, scientific approach to regulating novel technologies.

The challenge lies in maintaining public safety, whilst at the same time allowing the development of new technologies and their possible benefit to public health. It is of paramount importance to all involved — manufacturers, regulators and the public — that regulatory guidance, the provision of standards and the design of appropriate in-process tests keep pace with advances in science.

The World Health Organization is involved in promoting and facilitating the transfer of such science into the clinic, and in encouraging the global exchange of experience with these products. It plays a major role in developing internationally agreed written and physical standards. The efficient application of these standards forms a basis for the quality, safety and efficacy of biological medicines, as well as the reliability of diagnostic tests.

WHO's Biologicals Unit, within the Division of Drug Management & Policies, and the WHO Expert Committee on Biological Standardization develop guidance for national health authorities on the production and control of specific biologicals and, in collaboration with the WHO international laboratories for biological standards, establish WHO international reference materials against which batches of research materials or manufacturers' products can be assessed. WHO requirements and guidelines on biotechnology-derived biologicals include those for assuring the quality of recombinant DNA products, for monoclonal antibodies and for DNA-vaccines, as well as requirements for the use of animal cells as *in vitro* substrates for the production of biologicals.

Since 1992, the International Conference on Harmonisation (ICH) has also been active in drawing up guidelines on specific topics such as genetic stability, viral validation studies, and general product stability, with a view to improving the harmonization of regulatory decisions by the European Union, USA and Japan. Many of the ICH guidelines complement those produced by WHO.

Decisions on regulation and testing of biologicals and biotechnology products increasingly need to be made internationally for reasons of global and public health, international trade and the efficient use of national regulatory resources. Ways of improving and coordinating collaboration between national, regional and international agencies, and especially of supporting developing countries, need to be further explored, as do ways in which WHO can best promote such cooperation.

Many of the problems faced by regulatory agencies in meeting the challenges of biotechnology were discussed recently during the Eighth International Conference of Drug Regulatory Authorities (ICDRA) held in Bahrain. The Conference was organized by the Ministry of Health of Bahrain in collaboration with WHO (see page 182). Many of the complexities involved in the production of biotechnology-derived medicines were highlighted. These included differences in glycosylation between the same gene product expressed in different cells, or in the same cells under different growth conditions — differences which can have important consequences on product stability, *in vivo* distribution, and function. Also considered was the major problem of potential viral contamination — needing exhaustive testing of cell banks and well designed viral clearance studies to assure safety.

Clearly, these are highly sophisticated products which need an equally sophisticated and technically competent approach to regulation and testing. Considerable differences were apparent in experience in the regulation of biotechnology products between one country and another. The needs of countries with an evolving biotechnology industry are different from those that only import such products, and there is an obvious need to share expertise and transfer skills.

The conference recommendations relating to the challenge of biotechnology are given on page 184.

Reports on Individual Drugs

Post-malaria neurological syndrome and mefloquine

A comprehensive update on the safety issues related to mefloquine use in the prophylaxis and treatment of falciparum malaria was recently published in *WHO Drug Information* (1). Since that time, two informative studies have been published (2, 3) which explore further the adverse events associated with the use of mefloquine.

Observations made in Viet Nam and Thailand (2) that a discrete neurological syndrome appears after recovery from falciparum malaria have prompted a prospective four-year study of the post-malaria neurological syndrome (PMNS) in Viet Nam.

Of 18 124 patients treated for falciparum malaria, of whom 1176 had severe infections, 19 adults and 3 children developed subsequent PMNS 96 hours (median time) from parasite clearance after recovery from malaria. None of the patients had a previous history of neurological or psychiatric illness, but one patient was an intravenous drug-abuser and was HIV-positive. PMNS-defining manifestations were apparent in 13 (59%) patients, who had either an acute confusional state or an acute psychosis; 6 (27%) patients had generalized convulsions followed by an acute confusional state, and one patient developed fine tremor lasting 4 days.

Overall, 17 of the 22 patients with PMNS (77%) had been treated at some stage during their illness with mefloquine, 10 (45%) with quinine, 13 (59%) with a qinghaosu derivative (7 with artesunate and 6 with artemether), and 4 (18%) with pyrimethamine/sulfadoxine. The median time from the end of antimalarial treatment to onset of PMNS was 78 hours. Severe malaria PMNS developed in a further 16 of 412 known mefloquine recipients, compared with 4 of 764 patients who did not receive mefloquine (relative risk 7.4, 95% CI 2.5 to 22), and in one of 1012 patients who were prescribed mefloquine in uncomplicated malaria. All patients recovered from PMNS completely without specific treatment within ten days.

It was concluded that a strong association exists between treatment with mefloquine and the

development of PMNS, suggesting that mefloquine has a role in the etiology of this syndrome in most cases. The authors consider this risk unacceptable, and suggest that where an effective alternative drug is available, mefloquine should not be used for the treatment of severe malaria.

Acute self-limiting neuropsychiatric reactions to mefloquine have been well described in the context of both malaria prophylaxis and treatment (1). These observations are supported from Thailand where eight neuropsychiatric reactions were reported in a series of 13 950 supervised mefloquine treatments, giving an incidence of 0.57 per 1000 mefloquine-treated patients (4).

In a further study, mefloquine prophylaxis in 46 young healthy adults did not produce neurological dysfunction, but the subject population was small (3). During the study, however, transient mild QTc prolongation was reported, supporting the recommendation that halofantrine, which is also known to prolong the QT interval, should not be used in persons who have recently received mefloquine.

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Hormone replacement therapy and venous thromboembolism

The increased risk of venous thromboembolism associated with current use of oral contraceptives has been extensively documented, but until now it

has been unclear whether similar side-effects are also associated with hormone replacement therapy (HRT). Three papers recently published in the *Lancet* provide substantial evidence that there is an increased risk of deep vein thrombosis and/or pulmonary embolism in women taking HRT. Two reports were of case-control studies (1, 2), and one was of a prospective study where information was obtained through questionnaires (3). The trend in each of the studies was similar, and the relative risk of venous thromboembolism appeared to be raised 2 – 4 fold in current users of HRT. The absolute risk of all venous thromboembolic complications was rather small, 16 or 23 excess cases per 100 000 women per year, and for pulmonary embolism alone 6 per 100 000 women per year. It has been estimated that mortality from thromboembolism is about 1 – 2%. One of the studies suggested that smoking did not modify the risk. In pulmonary embolism, mortality following the initial event varies with the extent of embolization, but a patient with normal cardiopulmonary status is unlikely to die unless the occlusion exceeds 50% of the pulmonary vascular bed. According to the three studies, the risk of venous thromboembolism disappeared after HRT was stopped and the risk was not different for the various types of preparations used.

However, the question remains as to whether the benefit of HRT outweighs the observed potential risk. There is documented evidence that HRT relieves menopausal symptoms and that long-term use prevents or delays osteoporosis. It may also protect against ischaemic heart disease and possibly prevent or delay the onset of Alzheimer disease. The new findings of this small increase in risk of venous thromboembolism may not change the overall positive risk/benefit balance of HRT. Nonetheless, there may be individual cases where the risks of HRT will exceed the benefits. Venous thromboembolic complications are likely to be greater in women with predisposing factors such as a personal or family history of deep vein thrombosis or pulmonary embolism, severe varicose veins, obesity, recent surgery, trauma, immobilization or prolonged bed-rest. In such cases the use of HRT should be considered with caution.

On the basis on the findings from all three studies and other available data, it is concluded that at this time there is no reason for alarm, and women without predisposing factors for venous thromboembolism should continue to take HRT.

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Amodiaquine: a case for reconsideration?

In the late 1970s, amodiaquine was used widely as an alternative to chloroquine, for both the treatment and prevention of malaria. However, in the mid-1980s, cases of agranulocytosis and hepatitis associated with amodiaquine administration in malaria prophylaxis were reported, resulting in an abrupt decline in use of the drug (1, 2). The frequency of agranulocytosis was subsequently estimated to be in the order of 1 in 2200 and serious hepatotoxicity as 1 in 15 650 (3). Fatal reactions were reported as 1 in 15 500 travellers taking the drug.

As a consequence of these findings, labelling of the product was modified to exclude prophylaxis as an indication and, in 1990, WHO no longer recommended the drug for use in malaria control programmes (4). In 1993, the WHO Expert Committee on Malaria rediscussed the issue and concluded that amodiaquine could be used for the treatment of malaria provided that risk of infection outweighs the potential for adverse drug reactions. However, the Committee did not recommend amodiaquine for first-line treatment (5).

The question of how to predict and assess the risk of infection in relation to potential adverse drug reactions in individual patients cannot be easily addressed, and countries have differed in their response to this advice. Several have banned amodiaquine, whilst others continue to use it as second or even first-line treatment for uncomplicated malaria (6). Moreover, in some countries amodiaquine is produced locally and is still widely available, being the cheapest antimalarial drug after chloroquine. Amodiaquine also has certain advantages over chloroquine as it is more palatable

and retains its efficacy in many areas where chloroquine resistance has been reported.

In light of the global debate on the usefulness of the drug, a systematic review was made of results from the 40 randomized clinical trials that have been carried out on its effectiveness and safety thus far (6). In the treatment of uncomplicated falciparum malaria, amodiaquine proved to be significantly more effective than chloroquine. Time to parasite clearance was shorter with amodiaquine and fever clearance times were marginally faster. In comparative trials, amodiaquine and sulfadoxine/pyrimethamine were equally effective on day 7, but on day 14 and 28 sulfadoxine/pyrimethamine was slightly better, although fever clearance times were significantly shorter with amodiaquine. No life-threatening adverse events or significant shifts in laboratory parameters were reported, and the rates of adverse events in controlled clinical trials were 10.7%, 8.8% and 14.3% using amodiaquine, chloroquine and sulfadoxine/pyrimethamine respectively.

The review group requested supplementary safety data from the WHO Collaborating Centre for International Drug Monitoring in Uppsala and from the Parke-Davis data base. Some overlap in reported cases in these two data bases was evident. The WHO Collaborating Centre had re-ceived 28 reports between 1970 and 1994 on adverse events affecting white blood cells and the reticuloendothelial system in association with amodiaquine, including 17 cases of agranulocytosis and 7 of granulocytopenia. There were also 21 reports of adverse events affecting the liver and biliary system. Agranulocytosis and granulocytopenia occurred at an average 9 weeks (range 3 – 360 days) after initiation of amodiaquine treatment. In cases of agranulocytosis alone, time to onset varied from 48 to 98 days. The Parke-Davis data from 1985 to 1991 included 42 serious adverse events reported in association with amodiaquine chemoprophylaxis. There were 28 cases of agranulocytosis (of which 9 were fatal) and 14 of hepatitis (of which 3 were fatal). Amodiaquine intake varied between 200 and 700 mg per week for 3 to 48 weeks. No information on the frequency of these reactions was given, obviously due to the lack of data on the total number of drug users.

In short, the review provided evidence that amodiaquine is superior to chloroquine in the treatment of uncomplicated malaria in areas of chloroquine resistance. However, amodiaquine may only be marginally better than chloroquine in practice and, over time, resistance could negate its advantages

(7). In comparison to sulfadoxine/pyrimethamine, the rapid clinical action of amodiaquine retains relevance.

Unfortunately, the safety review could not provide enough conclusive data, and it remains to be seen whether the risks of agranulocytosis or severe hepatic toxicity are significantly lower when amodiaquine is used for treatment rather than prophylaxis. Clarification has not been provided on the risk of agranulocytosis and whether it is greater during the first weeks of treatment — as is usual in drug-induced agranulocytosis — or whether a preceding signal of neutropenia can be detected with regular laboratory tests. The possibility remains that amodiaquine induces an idiosyncratic-type reaction which is not predictable as a dose- or duration-related event. It is also not known if discontinuation of the drug in this phase can save the patient from severe or fatal agranulocytosis and no data are available on whether re-exposure to amodiaquine significantly increases the risk of agranulocytosis.

Further investigation of reported adverse drug reactions could possibly throw light on some of these doubts. Whatever the outcome, if amodiaquine is introduced again, this should be through "monitored release" — which will allow intensive surveillance of its efficacy and safety through carefully designed prospective studies.

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Safety Issues

Documentation requirements for approval: safety

Clinical information on the efficacy and safety of a new drug, which is submitted to a drug regulatory authority when requesting marketing approval, is developed through an orderly process of expanding investigations. This is done by progressively incorporating greater numbers of patients into studies of increasing length.

The main body of information is normally collected in phase II and III clinical trials during drug development. It is the case, however, that rare, unexpected, and occasionally severe adverse events can only be detected during post-marketing phase IV activities. Until now, the minimum information required by regulators when evaluating a product for marketing approval has varied considerably from country to country.

The International Conference on Harmonisation (ICH) has now debated the issue of documentation requirements during a series of meetings of the expert working group for efficacy. It has subsequently finalized a guideline to be applied in the countries of the ICH (European Union, Japan and the United States of America). The guideline is applicable to products intended for the long-term treatment of non-life-threatening diseases. This is defined as either continual or repeated intermittent use of a product for longer than six months. The guideline also points out that a distinction should be made between clinical data on adverse drug events derived from studies of shorter duration of exposure, and data from studies of longer duration. It is expected that short-term event rates (cumulative 3-monthly incidence of about 1%) will be well characterized. However, safety studies carried out during early clinical trials are not expected to identify rare adverse events such as those occurring in fewer than 1 in 1000 patients.

The working group, which includes experts from both regulatory agencies and the pharmaceutical industry, considered that the majority of adverse drug events are first sighted and are most frequent within the first few months of drug treatment. It was

agreed that the number of patients treated for six months at dosage levels intended for clinical use should be adequate to characterize the pattern of these adverse events. To achieve this objective, the cohort of exposed subjects should be large enough to observe whether more frequently occurring events increase or decrease over time as well as to observe delayed events of reasonable frequency (e.g., in the general range of 0.5% to 5.0%). For this purpose, between 300 and 600 patients treated for a period of 6 months should normally be adequate.

However, although they are likely to be uncommon, it is a fact that some adverse events may increase in frequency or severity with time, and some serious adverse events may occur only after treatment for more than six months. Consequently, 100 observed patients exposed to dosage levels intended for clinical use for a minimum of one year is considered to be appropriate. If no serious adverse drug event is observed in a one year exposure period, this number of patients provides reasonable assurance that the true cumulative one-year incidence is no greater than 3%.

The working group concluded that the cumulative total number of individuals treated with an investigational drug, including short-term exposure, should be about 1500. Since Japan currently accepts between 500 and 1500, it is evident that it has not been easy to reach a final decision upon the precise number of exposed patients which is acceptable for safety documentation requirements. This difficulty is reflected in several exceptions that have been listed at the end of the guideline as follows.

More data are required:

- where data from animal studies signal a possible adverse event;
- where indicative clinical information is available from other agents with a related chemical structure or from a related pharmacological class;
- where pharmacokinetic or pharmacodynamic properties of the product are known to be associated with an adverse drug event;

- when a specific serious adverse event has been identified in similar drugs or where a serious event that could represent an alert event is observed in early clinical trials;
- where the benefit from the drug is either small or will be evident only for a fraction of the treated patients or is of uncertain magnitude (surrogate endpoints as determinants for efficacy); and
- when there is concern that a drug may add to an already significant background rate of morbidity or mortality.

Finally, the guideline states that in exceptional cases a smaller number of patients may be acceptable — for example, where the intended treatment population is very limited.

It is expected that regulators and the pharmaceutical industry will welcome this guideline. Experience collected from its future application should simplify and clarify its complexity, resulting in a final consensus document that will be recognized by the regulatory community worldwide.

Reference: The extent of population exposure to assess clinical safety for drugs intended for long-term treatment of non-life-threatening conditions. ICH harmonised tripartite guideline. In: *Proceedings of the Third International Conference on Harmonisation*. Yokohama, 1996.

Drug safety monitoring centres

A drug safety monitoring programme only makes sense if the responsible authority can take regulatory action when a drug is identified as having safety problems. For this reason, regulatory agencies often consult their national drug monitoring centres for information on the safety profile of a product during the drug approval process and as required in the post-marketing phase.

At the request of its Member States, WHO has established a network of national centres under the aegis of the WHO International Drug Monitoring Programme. This Programme is supported by the

WHO Collaborating Centre for International Drug Monitoring in Uppsala, Sweden, where a data base of almost two million reports is housed. The data base is accessible to a network of 50 national centres which depend on this information to confirm or disprove suspicions at national level.

WHO serves to establish, promote and maintain collaboration between the national centres which currently make up the programme. It gives assistance to countries in establishing and running an effective national safety monitoring system. WHO also organizes annual meetings which bring together representatives of the national centres. This year's meeting was held in Lisbon and was hosted by the Ministry of Health of Portugal and the national drug safety programme, INFARMED. Over ninety participants attended the meeting, including representatives from candidate countries wishing to establish a national centre.

The agenda covered discussion of recent reports of adverse drug reactions that have the potential to become major signals, including events following vaccination. This gives early warning to drug regulatory authorities to consider restrictive measures.

The abuse liability of a drug is not easily established and the WHO Programme on Substance Abuse hosted a special session to address this issue. A unified policy in identifying drugs with potential dependence liability was called for.

During the past five years, reports have been received from several countries on the intoxication of hundreds of children with diethylene glycol, used instead of propylene glycol as a solvent for the preparation of paediatric cough syrup. Attention was drawn to the WHO project on counterfeit drugs, and national centres were called on to report cases to WHO of undue toxicity, as well as the absence of therapeutic activity in products.

Various other topics of interest were discussed, such as the ICH common terminology and its impact on the programme's own reporting system and terminology. The next meeting will be held in Geneva in September 1997.

General Information

Recommendations from the ICDRA reinforce the mission of regulatory authorities

Over 150 government regulatory officials and experts, representing more than 90 countries, were united recently at the Eighth International Conference of Drug Regulatory Authorities (ICDRA) which took place in Manama, Bahrain. The Conference was co-sponsored and organized by the Ministry of Health of Bahrain in collaboration with WHO's Division of Drug Management and Policies (DMP).

Participants at the Conference reiterated the core mission of drug regulatory authorities to promote public health and ensure the quality, safety and efficacy of pharmaceutical and biological products. In the current climate of rapid development and marketing of new products and technologies, the safe and rational use of health-related products and medicines was recognized as fundamental.

The conference provided a forum for discussion and debate of those regulatory issues which provide a daily challenge to many national authorities. These issues include the question of counterfeit drugs, regulatory control measures, safety monitoring, biotechnology, control of herbals and multisource (generic) products and the international harmonization process. Time was also allowed for free discussion of various current topics, and links were established among many of the regulatory authorities which were represented at the Conference.

Nine specific and two open-discussion sessions led to the formulation of the following general recommendations:

International harmonization of regulatory requirements

1. Globalization of ICH (International Conference on Harmonisation) documents is vital and WHO, together with ICH, should investigate ways in which this can be carried out.

2. In order to avoid disharmony, WHO should utilize, as appropriate, ICH guidelines in drafting its own normative global guidelines.

3. WHO, in collaboration with ICH, should establish mechanisms to integrate ICH products into WHO regional educational and training activities on harmonization.

4. ICH final (Step 4) and draft (Step 2) guidelines should be distributed widely and be available on Internet. Feedback on the guidelines should be accommodated through an electronic mail-box, in addition to the usual written procedures.

5. Because of the complex issues related to World Trade Organization (WTO) agreements such as the Agreement on trade-related aspects of intellectual property rights (TRIPS) and Technical Barriers to Trade, WHO should continue working with WTO based on the mandate of WHA resolution 49.14 (Item 10) on the Revised Drug Strategy to clarify and rapidly inform drug regulatory authorities about their implications.

6. Discussion on regional, international and global harmonization activities related to medicinal products, including ICH, should remain on the agenda of each ICDRA. Reports on WTO issues related to pharmaceuticals, including TRIPS and Technical Barriers to Trade, should also be covered in the sessions.

The mission of drug regulatory authorities

Mission of drug regulatory authorities

Drug regulatory authorities (DRAs) should have a written mission statement which provides a concise, challenging, inspiring vision of what the DRA stands for and what it means to achieve. The core mission for all DRAs is to promote public health by ensuring the quality, safety, and efficacy of pharmaceuticals. Depending on the country, the mission may also include:

- providing unbiased information and promoting safe, effective use of drugs.
- ensuring timely availability of drugs (prompt authorization decisions).
- supervision of the distribution chain.
- stimulating innovation of new medicinal products.

Structure and financing

The structure, staffing, financing and operation of a DRA must be suited to its mission. This may require innovative measures such as establishing a (semi) autonomous agency, implementing user fees for DRA services, and contracting specific functions to nongovernmental bodies.

Independence in decision-making

Independent, autonomous decision-making by DRAs must be backed by appropriate legislation.

Guidelines based on health needs

International guidelines for drug quality, safety, efficacy, and information — including those produced by WHO and ICH — should be based on what is clinically necessary, not simply what is technically possible. Guidelines should be driven primarily by health considerations, not by ever-expanding technology.

Electronic information exchange

In collaboration with WHO, regional and global electronic networks for the exchange of regulatory information similar to the drug information services currently provided in “hard copy” by WHO/DMP should be set up. DRAs in Member States should provide WHO with information on important and significant developments that may be useful to other countries.

Financing of drug regulatory authorities

Financing must be adequate and continuously guaranteed to ensure smooth running of the DRA. Financing options include (a) government financing, (b) user fees, or (c) a combination of the two funding sources. Regulatory fees should be based on the real cost of providing DRA services, including drug evaluation, licensing, inspection, quality control testing, etc. It is preferable that a suitable amount of the fees collected for drug regulation services is retained to finance costs of the DRA.

Enforcement of drug control

Legislation and regulation of drugs must be backed up by adequate enforcement mechanisms (staff, authority), sufficient public/political support, and firm penalties for offences.

Veterinary drugs and DRAs

Because use of veterinary drugs can have direct and indirect effects on human health, Member States should ensure that there is clear and specific responsibility for the registration and quality assurance of veterinary drugs, and for establishing and monitoring maximum residual limits.

Drug information and ethical promotion

DRAs must have the legislative mandate and the necessary mechanisms to ensure accurate drug information and ethical drug promotion. Agreements with industry on advertising rules and the nomination of designated responsible professionals within industry could enhance the effectiveness of regulatory control.

Pharmaceutical products are not commodities and uncontrolled sales through electronic means (Internet) may carry a high risk. WHO should address distance selling and promotion via the Internet, and application of the *WHO Ethical Criteria for Medicinal Drug Promotion* should be made to such activities.

Counterfeit drugs

1. Awareness should be improved of the growing problem of counterfeit drugs in terms of public health, both nationally and internationally.
2. WHO should coordinate the creation of a network of technically competent officials in order to ensure timely exchange of information, both on cases of counterfeits as well as on countermeasures.
3. WHO should develop a model text for specific and strong legislation. Penalties should be firm enough to have a deterrent effect.
4. WHO should develop indicators, for use within a national drug policy, for estimating the problem of counterfeit drugs.
5. Since many of the problems with counterfeit drugs are similar to those with narcotic drugs, WHO should establish close collaboration with the International Narcotics Control Board.
6. Health authorities should try to monitor free ports more intensively.
7. Collaboration between DRAs and law enforcement agencies should be strengthened.
8. Pharmaceutical companies should be prepared to share their information. This information should be handled with due discretion to avoid loss of confidence in genuine products.
9. Companies should be more cautious in sales procedures with regard both to the purchase of starting materials and the introduction of the products into the distribution chain.

10. Although there is a difference of definition between counterfeit and substandard drugs, WHO and DRAs should concentrate on the prevention of both.

Computer-assisted drug registration

1. The training activities that accompany the provision of the WHO software for computer-assisted drug registration should be tailored to the actual specific needs of country staff and their regulatory experience.
2. Countries should help WHO to identify resources to permit all the necessary assistance to be provided for implementation of the computer-assisted system until staff have acquired the necessary familiarity, and adaptations have been completed and the system is put into routine use.
3. More effort should be put into developing regional and subregional reference centres that can provide sustained assistance to interested countries.

The challenge of biotechnology

1. WHO, in collaboration with the ICH or as appropriate, should continue to develop clear guidelines on issues relating to the quality, safety and efficacy of biotechnology-derived medicinal products.
2. National control authorities lacking experience in the regulation of biotechnology-derived products should be strengthened through education, training and updating, as appropriate. They should draw upon the knowledge and skills of national control authorities already well experienced in this area, in collaboration with WHO.
3. National control authorities with limited expertise should identify potential alternative sources of expertise within their countries to assist in the review of licence applications for bio-technology products and for undertaking laboratory testing. Where these are lacking, regional collaboration should be explored as a means of obtaining the necessary skills and knowledge. WHO should facilitate such regional cooperation.
4. WHO should strive to improve awareness and dissemination of guidance documents, especially to developing countries, including ICH guidelines which are complementary to WHO guidelines.

5. The development of physical reference preparations that can serve as reference standards for new products is considered an important function of the WHO Biologicals Programme and should be continued.

Pharmacovigilance

1. The feasibility of establishing a reporting system for medication errors should be investigated.
2. Collaboration of the national monitoring centre with other institutions should be strengthened. Such institutions include: WHO and its Collaborating Centres, the local drug and poison information centres, universities, drug formulary commissions, manufacturers, the media, and consumers.
3. Considering the need for qualified staff. WHO should coordinate the organization of regional or sub-regional training courses in pharmacovigilance which are tailored to the local medical and linguistic situation.
4. Pharmacovigilance should be included in university curricula and postgraduate courses of medical as well as pharmaceutical education.
5. DRAs should make resources available to national monitoring centres to enable them to carry out, sponsor, or participate in scientific research.

WHO Certification Scheme: current developments

1. Application of the WHO Certification Scheme for drugs intended to be imported should be made mandatory through relevant regulations. WHO-type product and batch certificates should become part of the documentation to be submitted when applying for a marketing authorization.
2. Drug regulatory authorities should not insist on authentication of WHO-type product certificates issued by the drug regulatory authority in the exporting country, and all DRAs should request their office of foreign affairs/trade to instruct their embassies accordingly.
3. Countries that now delegate the issuance of WHO-type certificates to state authorities should recognize the difficulties this presents in building up trust in the importing countries.

4. Drug regulatory authorities in importing countries should contact their counterpart in the exporting country, particularly if an applicant is unwilling to provide the requested WHO-type certificate.

5. The IFPMA, WFPMM, and national and regional manufacturers' associations should instruct their member companies to include WHO-type certificates in their documentation when applying for registration of a product in the country to which the product is to be exported.

6. Users should bring to the attention of WHO any problems encountered in the use of the Scheme so that it can be further improved.

Regulatory control and assessment of herbal medicines

1. Member States should encourage research on the use of herbal medicines, especially clinical trials.

2. WHO, in collaboration with governments, NGOs, institutions and collaborating centres, should continue to develop and review technical documents dealing with herbal medicine, and should encourage Member States to establish groups of experts on herbal medicines in their own countries or regions.

3. WHO should continue to compile knowledge on the safety and efficacy of herbal medicines, including further development of the Model Monographs on Widely-Used Medicinal Plants.

4. WHO should assist Member States in organizing training programmes for the regulation and evaluation of herbal medicines.

5. WHO should continue to update guidelines on the assessment of the quality, safety and efficacy of herbal medicines.

6. WHO should also prepare similar criteria in related fields of traditional medicine.

Registration requirements for multisource products (generics)

Drug regulatory authorities should consider the following possibilities when evaluating multisource products:

- establish criteria on requirements for comparative data on pharmaceutical equivalence;

- establish lists of substances for which *in vivo* bioavailability/bioequivalence studies are required;

- establish a list of substances for which *in vivo* bioavailability/bioequivalence studies are not required; and

- establish lists of products where substitution in an individual patient may be a problem.

WHO should:

- continue to provide guidance on the selection of comparator products;
- closely follow developments at national level intended to limit the need for *in vivo* studies; and
- look into the possibility of developing model drug registration dossiers for specific essential drugs with a potential for bioavailability problems.

Regulatory measures to allow timely provision of controlled medicines in emergency situations

1. National drug regulatory authorities should consider applying, on a trial basis, simplified regulatory measures to allow for the timely provision of controlled medicines in emergency situations as proposed in the *Model guidelines for the international provision of controlled medicines for emergency medical care**, which may be adapted or modified to meet national requirements.

2. WHO should review experience gained from this trial implementation at an appropriate time in the near future.

The objectives of the Conference — to forge a consensus on matters of mutual interest, to facilitate timely and adequate exchange of technical information, and to discuss contemporaneous issues of international relevance — were once again achieved.

The conference concluded with an announcement that the Ninth International Conference of Drug Regulatory Authorities will be hosted by the Ministry of Health of Germany, and will take place in Berlin in April 1999.

* World Health Organization. *Model guidelines for the international provision of controlled medicines for emergency medical care*. Document WHO/PSA/96.17. WHO, Geneva.

***The International Pharmacopoeia* — how useful is it?**

The International Pharmacopoeia, which was established by the first World Health Assembly in 1948, sets out recommended procedures of analysis and specifications for pharmaceutical substances, excipients and dosage forms. The pharmacopoeial monographs described are mainly based on the drug products contained in the *WHO Model List of Essential Drugs*.

One of the basic aims of *The International Pharmacopoeia* is to offer an alternative to the often very sophisticated and expensive methods described in other pharmacopoeias. In this way, countries which do not have the means to carry out these methods are nonetheless able to assure international standards of quality.

It was considered timely to evaluate the exact role of *The International Pharmacopoeia*. Is it still required? And, if so, how many Member States are using it today? With this in mind, a tear-off questionnaire was attached to each copy of *The International Pharmacopoeia* published in 1994. The same questionnaire was also distributed to interested institutions in WHO Member States with the intention of assessing the utility, degree, and pattern of use. Replies were received from 88 countries out of a total of 190 Member States (46%). These covered all six WHO Regions.

In summary, 99% of the replies stated that *The International Pharmacopoeia* is used for multiple purposes. Sixty per cent of the replies showed that in 65 Member States, covering both developed and developing countries, it is most typically used as a reference tool for the development of national standards. It is also widely used for day-to-day quality testing of imported pharmaceutical products in 62 countries, and for locally manufactured drugs in 53 as well as for teaching material in 56 countries. Other uses of *The International Pharmacopoeia* include: adoption as national pharmacopoeial or similar standards (mostly in developing countries), and in product licensing or procurement of pharmaceuticals. Details of the various uses indicated in the replies, giving the total number of answers received for each use, can be obtained upon request from the Quality Assurance

Unit of the Division of Drug Management & Policies, WHO, 1211 Geneva 27, Switzerland.

Reference preparations for the evaluation of diagnostic kits used in blood screening

Reliable and sensitive tests for the detection of hepatitis B surface antigen (HBsAg), and antibodies to hepatitis C (HCV) and HIV are essential for the safety testing of blood used for transfusion and in the preparation of blood derivatives such as factor VIII and immunoglobulins.

Diagnostic kits used in the screening process need to be standardized to ensure reliable and comparative results internationally. In order to discuss the development of international WHO reference preparations and evaluation material which could be used to test the performance of kits as part of their quality control, a consultation was recently organized by WHO. Participants at the meeting included representatives from the six WHO regions.

A review of the current situation revealed that there are several reference reagents used in different countries, but no internationally accepted standards for the detection of anti-HCV and anti-HIV antibodies yet exist. It was also not clear whether the existing WHO international standard for HBsAg meets current needs. Fundamental parameters to evaluate the kits would be sensitivity, specificity, reproducibility, and stability.

The ideal would be to develop a globally agreed reference panel that would be freely available to all control laboratories. However, given the distinctive needs of countries and the different structure and levels of development of screening services, as well as the time needed to develop a fully operational system, these reference materials may only be useful in complementing the existing systems for the time being.

In view of the major obstacles involved in this task, a working group has been set up to oversee the development of WHO reference preparations. The first meeting of the working group was held very recently at WHO in Geneva.

Regulatory Matters

Acellular pertussis vaccine for infants

United States of America — The Food and Drug Administration has approved the first acellular pertussis vaccine for use in infants and children aged two months and older for primary immunization. While the vaccine protects infants against whooping cough, it causes fewer side-effects than whole-cell pertussis vaccines.

Acellular pertussis vaccines contain only those parts of the pertussis bacterium which are thought to be important for immunity, while whole-cell vaccines contain the whole killed bacterium.

Reference: *HHS News*, P96-12, 31 July 1996.

Breath test for *Helicobacter pylori*

United States of America — A breath test (Meretek UBT Breath Test Collection Kit®, Meretek Diagnostics, Inc.) to detect *Helicobacter pylori* bacterium, which is associated with duodenal ulcer, was cleared for marketing by the Food and Drug Administration in September 1996.

It is hoped that the new test will be useful in simplifying diagnosis, which normally requires endoscopy and stomach biopsy — a procedure in which the patient often needs to be sedated. With the new breath test, the patient first drinks a non-radioactive diagnostic drug solution of naturally occurring carbon 13-enriched urea (Pranactin®), and then exhales into the collection kit. This procedure can be performed in a physician's office and takes about 30 minutes. Following this, the breath kit is sent to Meretek for analysis, and the results are available in one or two days.

The FDA's approval was based on data from studies in 499 adults with duodenal ulcer which showed that the breath test was able to detect the presence of *H. pylori* in 95% of cases. This is similar to the detection rate with biopsy.

Reference: *FDA Talk Paper*, T96-72, 1 November 1996.

Restrictions on use of anorectics

European Union — During 1995 and 1996, the Committee for Proprietary Medicinal Products (CPMP) carried out a risk-benefit evaluation of the following centrally acting anorectic drugs: fenfluramine, dexfenfluramine, amfepramone, clobenzorex, fenproporex, phenmetrazine, fenbutrazate, mazindol, mefenorex, norpseudoephedrine (INN=cathine), phentermine, phendimetrazine and propylhexedrine. The assessment focused on the efficacy and safety of the products and considered, in particular, the risk of severe, often fatal pulmonary hypertension that has been reported in some patients receiving anorectics.

As a result of this assessment, the benefit-risk ratio for use of anorectics was considered to be favourable only when:

- use is restricted to major obesity, i.e. a body mass index (BMI) of 30 kg/m² or higher;
- anorectics are used as second-line therapy in patients who have not responded to an appropriate weight-reducing regimen alone;
- the duration of treatment takes into account the risk of pulmonary hypertension, which has been shown to increase beyond three months;
- clear information on the potential fatal risk of pulmonary hypertension-related anorectic intake is made available to both physicians and patients; and
- the product is administered by a physician experienced in the treatment of obesity.

The CPMP stressed the importance of careful compliance with the indications and due regard to the duration of treatment.

Reference: *CPMP Assessment Report for Anorectic Agents*. CPMP/127/96 Rev. 6, 18 July 1996.

France — The French Medicines Agency has established a new prescribing status for the anorectic serotonergic compounds dexfenfluramine

and fenfluramine, and the anorectics amfepramone, clobenzorex, fenproporex and mefenorex.

In the future, these products should be prescribed by a specialist physician and used only in patients with major obesity, for a treatment period not exceeding 3 months.

The Agency has taken this action following analysis of 78 reported cases in France of pulmonary hypertension. These were selected by an expert pneumologist from a total of 117 reported cases. The outcome was known for 63 cases, among which were 23 deaths, 14 with dexfenfluramine, 4 with fenfluramine, 4 with amfepramone and 1 with clobenzorex. Four patients required lung transplantation — three had taken dexfenfluramine and one fenfluramine. Eight patients were waiting for lung transplantation, of whom 6 had been treated with dexfenfluramine and 2 with fenfluramine. Of the remaining cases, 3 patients treated with dexfenfluramine had improved, but 25 patients had not yet recovered.

References

1. Avis aux prescripteurs, 10 mai 1995.
2. Letter of 10 October 1996 to WHO from the Agence du Médicament, France.

Canada — In a letter to physicians (1), the Department of Health and Welfare has warned that pharmaceutical products containing fenfluramine are indicated only for short-term use — no longer than three months — because of a 23-fold increase in the risk of primary pulmonary hypertension (PPH) that has recently been reported in the *New England Journal of Medicine* (2).

The Agency states that the long-term efficacy of these products has not been established, and that indications for all appetite suppressant drugs have been restricted to the medical management of obese patients with a minimum body mass index of 30 kg/m².

Primary pulmonary hypertension occurs in the general population at one to two cases per million adults per year, while the estimated risk in patients taking appetite-suppressant drugs for longer than three months is 23 to 43 cases per million patients per year. PPH is a life-threatening condition with an estimated four-year survival rate of 55 per cent.

References

1. Dear Doctor letter from Health Protection Branch, Canada, dated 21 October 1996.
2. Abenheim, et al. *New England Journal of Medicine*, **335**: 609–616 (1996).

United States of America — Following the final report of the International Primary Pulmonary Hypertension Study (IPPHS), the Food and Drug Administration has requested the manufacturer and the distributor of dexfenfluramine products to revise the product information and inform physicians and patients of the increased risk of primary pulmonary hypertension (PPH) which is a rare, but serious and life-threatening disorder. The FDA approved dexfenfluramine for the treatment of obesity in April 1996.

Letters have since been sent to more than 300 000 health care providers, including some 155 000 physicians, advising that the new findings on the higher risk of PPH associated with use of appetite suppressants reinforce advice that dexfenfluramine should not be used for “cosmetic” weight loss. This product should be used only in patients whose body mass index (BMI) is at least 30 kg/m². Patients with other risk factors, such as hypertension or diabetes, can be treated with the drug if their BMI is 27kg/m² or higher.

The FDA also requested that updated information on the risk of PPH should be included in the product information and in the patient package insert, allowing patients to make an informed choice about whether or not to take the drug.

The FDA emphasizes that any appetite-suppressant drugs should be taken only under careful supervision, and suggests that treatment should be discontinued if a patient develops unexplained symptoms including shortness of breath or difficulty in breathing, angina pectoris, syncope or oedema in the lower limbs.

Reference: *FDA Talk Paper*, T96-58, 22 August 1996.

Coumarin: regulatory action

Australia — The Australian Drug Evaluation Committee has received 10 reports of patients who developed abnormalities in liver function tests or more serious signs of hepatotoxicity (including two

fatal cases) associated with the use of tablets containing 200 mg of coumarin. Consequently, in August 1996, the health authorities cancelled registration of coumarin.

Coumarin is chemically related to the 4-hydroxy-coumarin anticoagulants, including warfarin, but it has no anticoagulant activity. It is used in the treatment of lymphoedema and was developed in Australia.

Reference: Letter from the Therapeutic Goods Administration to WHO, August 1996.

New Zealand — The Ministry of Health has sent a "Dear Doctor" letter to physicians informing them of the findings and decision made in Australia concerning coumarin. The product in question has not been approved for marketing in New Zealand, but it is being prescribed under the Medicines Act for treatment of lymphoedema.

Reference: *Prescriber Update*, 11: 19 (1996).

Switzerland — Two more cases of hepatotoxicity linked to coumarin administration have been reported to the Intercantonal Office for Medicines Control (OICM). Information on three previous cases, which were confirmed on rechallenge, have also been received by the pharmacovigilance centre.

In light of these and other findings from Australia, the risk/benefit profile of coumarin is currently under review by the Swiss OICM, and regulatory measures are expected in the near future.

Reference: *Bulletin des Médecins suisses*, 77: 1349 (1996).

Laxatives: reclassification of common ingredients

United States of America — The Food and Drug Administration has requested manufacturers of laxatives to provide additional data on the safety of over-the-counter products containing phenolphthalein, bisacodyl, aloe, cascara and senna. Laboratory data indicate that some of these components may have carcinogenic potential or mutagenic effects. However, no adverse reaction reports have been received so far concerning these substances.

Reference: *FDA Talk Paper*, T96-37, May 1996

Is melatonin a prescription drug?

United Kingdom — The Medicines Control Agency (MCA) has determined that products containing melatonin are medicinal by function and require marketing authorization, as their primary purpose is the remedy of sleep disorders such as jet-lag.

References

1. Letter from the Medicines Control Agency to WHO, 15 July 1996

2. *The Pharmaceutical Journal*, 255: 537 (1995).

Germany — The Federal Institute for Consumer Protection and Veterinary Medicine has decided that products containing melatonin require a marketing authorization in line with other pharmaceutical products within the country.

Reference: *Pressedienst*, 13/96, 14 June 1996.

Denmark, Norway and Sweden — Drug regulatory authorities in Denmark, Norway and Sweden have classified melatonin as a drug and Norway has classified melatonin-containing products as prescription medicines.

Reference: *Nytt om legemidler*, 19: 56 (1996).

Finland — The National Agency for Medicines has classified melatonin products as prescription drugs.

Reference: *Tabu*, 2: 41 (1996).

NSAIDs, antimicrobials and angioedema

Malaysia — Between 1990 and 1995, the Malaysian Adverse Drug Reaction Advisory Committee received a total of 56 reports of angioedema. A review of the reports indicated that use of non-steroidal anti-inflammatory drugs (NSAIDs) was associated with 24 reports, co-trimoxazole 13, and antibiotics 13. The most implicated NSAIDs were diclofenac (13), acetylsalicylic acid (7), indometacin (5), ibuprofen (2) and tiaprofenic acid (1).

Reference: *Berita Ubat-Ubatian*, 10: 11 (1996).

Drug-induced liver disease

Australia — The Australian Drug Evaluation Committee has expressed its concern about the

high number of reports on adverse hepatic reactions associated with the use of flucloxacillin and amoxicillin/potassium clavulanate products.

The Committee has reminded physicians to prescribe amoxicillin/potassium clavulanate only when it is clearly indicated, and to exercise particular care with its use in elderly patients.

Reference: *Australian Adverse Drug Reactions Bulletin*, 15: 6 (1996).

Fluoxetine and hepatitis

Spain — Several cases of hepatitis and raised transaminase levels have been reported in patients treated with the antidepressant fluoxetine.

Since this product belongs to a group of drugs not generally associated with hepatic reactions, the Catalan Institute of Pharmacology has requested collaboration from doctors in monitoring and reporting any such events.

Reference: *Butlletí groc*, 9: 8 (1996).

Hepatitis B vaccine and musculoskeletal reactions

Australia — Between 1988 and 1996, the Australian Drug Evaluation Committee received some 600 reports of suspected adverse reactions following hepatitis B vaccination. The most common reactions were rash and/or itch (181), anorexia, nausea or vomiting (131), musculoskeletal symptoms such as arthritis, arthralgia and myalgia (106), fever and/or rigor (99), headache (96), injection site reaction ((9), and dizziness and/or vertigo (64).

Reference: *Australian Adverse Drug Reactions Bulletin*, 15: 6 (1996).

Pyrithyldione-diphenhydramine and agranulocytosis

Spain — Between 1980 and 1995, the Pharmacovigilance Centre of the Catalan Institute of Pharmacology received some 280 reports of agranulocytosis. Of these, nine were associated with use of a combination hypnotic-sedative product, pyrithyldione and diphenhydramine.

Although evidence is weak, the Centre suspects that agranulocytosis may have been caused by pyrithyldione, and warns that the benefit-risk profile of this product may be unfavourable as a consequence.

Reference: *Butlletí groc*, 9: 6 (1996).

Roxithromycin associated with cardiac arrhythmias

New Zealand — The Centre for Adverse Drug Reaction Monitoring has received four reports of palpitations and/or tachycardia associated with the use of the macrolide antibiotic roxithromycin. One additional report presented cardiac arrest with ventricular fibrillation in a 31-year-old woman with no other apparent risk factor.

Another macrolide antibiotic, erythromycin, is also known to have been associated with dose-dependent pro-arrhythmic effects.

Reference: *Prescriber Update*. 11: 17 (1996).

Recent Publications

WHO Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-fourth report

This report sets out a series of twelve international guidelines and other recommendations intended to assist national drug regulatory authorities and manufacturers in the quality control of pharmaceutical products. Concerns addressed include the need to ensure that pharmaceutical products moving in international commerce are of acceptable quality, that generic drugs are therapeutically equivalent to innovator products, and that drugs retain their quality, safety, and efficacy throughout their designated shelf-life, particularly under the extreme climatic conditions often found in developing countries. The report also responds to the need to extend previously issued WHO guidelines for good manufacturing practices (GMP) to cover several special circumstances.

Although the report has universal relevance, its guidance is of particular importance in countries attempting to establish or strengthen a regulatory framework for pharmaceutical products. All recommendations share the ultimate goal of assisting regulatory authorities to safeguard the health of patients by protecting them from substandard or counterfeit products.

Two of the guidelines focus on premarketing studies, covering the technical data that should be included in the registration dossier when applying for a marketing authorization. The most extensive guidelines, on multisource pharmaceutical products, address the need to ensure that generic drug products satisfy the same standards of quality, efficacy and safety as those applicable to the originator's product and that adequate comparative studies have been conducted to verify whether the products are interchangeable. Presented in seven parts, the guidelines provide global standards and requirements for the regulatory assessment, marketing authorization, documentation of therapeutic equivalence, and quality control of multisource products.

The second guidelines, on stability testing of pharmaceutical products containing well-established drug substances, specify the tests needed to predict the stability of a drug product and determine its shelf-life and storage conditions in various climatic zones. The availability of these WHO guidelines is considered to be of special importance for testing products for use in the more extreme climatic conditions found in many developing countries, because such advice is lacking in other guidelines.

The report also contains revised guidelines for implementation of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, including standardized format and contents for product and batch certificates to be issued by the drug regulatory authority of the exporting country and the manufacturer.

Three guidelines supplement previously issued advice on good manufacturing practices (GMP), and cover the validation of the manufacturing processes, the manufacture of investigational products for clinical trials in humans, and the manufacture of herbal medicinal products. The resurgence of interest in herbal medicines is further reflected in guidelines for assessing their quality, safety and efficacy and for approving product labelling and package inserts. Other information includes updated lists of International Chemical Reference Substances and International Infrared Reference Spectra, supplemented by recommendations for the preparation and use of infrared spectra in pharmaceutical analysis. The report also contains extensive guidelines for the standardized graphic representation, whether hand-drawn or computer-assisted, of chemical formulae.

The report concludes with detailed guidelines on import procedures intended to promote efficiency in applying relevant regulations, to simplify the checking and handling of consignments in international transit, and to provide a basis for collaboration between the various regulatory, trade, customs, and port authorities. Full details of the

special controls required for narcotic drugs and psychotropic substances are also included

WHO Technical Report Series, No. 863, 1996. vi + 194 pages (available in English, French) ISBN 92 4 120863 5. Price: Sw.fr. 35.- (developing countries Sw.fr. 24.50)

Good pharmacy practice (GPP) guidelines

All practising pharmacists should be committed to their profession and ensure that the service they provide to each patient is of appropriate quality. A recent WHO document sets out the four basic principles of good pharmacy practice (GPP).

The *Good pharmacy practice guidelines* have been drawn up with a view to encouraging national pharmaceutical organizations to focus the attention of pharmacists in both the community and hospitals on developing the elements of the service they provide. Conditions of practice vary widely from country to country and each national pharmaceutical organization must decide what can be achieved. Such organizations should be particularly active in ensuring that pharmaceutical education is designed to equip pharmacists for the roles they have to undertake in hospital and community practice.

The present document is updated from the International Pharmaceutical Federation's (FIP) text of "good pharmacy practice" which was originally adopted during the World Congress of Pharmacy and Pharmaceutical Sciences in Tokyo in 1993. It sets out to provide a framework for the development of standards which follow closely the philosophy of good pharmacy practice. After a clear description of the framework of GPP, requirements are proposed covering health promotion and ill-health prevention, supply and use of prescribed medicines, and influencing prescribing and rational use of medicines.

These guidelines are recommended as a set of professional goals in the interest of patients and end-users at the pharmacy. All national pharmaceutical organizations are urged to implement them at the earliest opportunity.

Good pharmacy practice (GPP) in community and hospital pharmacy settings. PHARM/DAP/96.1. World Health Organization, Geneva. Available on request from Regulatory Support, Division of Drug Management & Policies, WHO, 1211 Geneva 27, Switzerland.

International Nonproprietary Names (INN) for pharmaceutical substances: cumulative list No. 9

This publication groups together the 6567 international nonproprietary names published by WHO up to December 1995. The list features INNs presented in alphabetical order under the Latin name and each entry includes equivalent names in English, French, Russian and Spanish. Also listed is the molecular formula and the corresponding Chemical Abstracts Service (CAS) registry number.

Three separate indexes allow retrieval of the INN equivalent in relation to the national name; the name of the substance from knowledge of its formula; or the name according to its CAS registry number. INNs for substances which are no longer marketed or which were abandoned before marketing are listed in an annex.

Procedures for the selection of recommended INNs, as well as the general principles for guidance in devising INNs, are also explained in length.

International Nonproprietary Names (INN) for pharmaceutical substances: cumulative list No. 9, 1996. xliii + 885 pages (bilingual English/French) ISBN 92 4 0560 16 5. Price: Sw.fr. 250.- (developing countries Sw.fr. 175.-)

International Nonproprietary Names for Pharmaceutical Substances (INN)

Notice is hereby given that, in accordance with article 3 of the Procedure for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances, the names given in the list on the following pages are under consideration by the World Health Organization as Proposed International Nonproprietary Names. The inclusion of a name in the lists of Proposed International Nonproprietary Names does not imply any recommendation of the use of the substance in medicine or pharmacy.

Lists of Proposed (1-73) and Recommended (1-35) International Nonproprietary Names can be found in Cumulative List No. 9, 1996. The statements indicating action and use are based largely on information supplied by the manufacturer. This information is merely meant to provide an indication of the potential use of new substances at the time they are accorded Proposed International Nonproprietary Names. WHO is not in a position either to uphold these statements or to comment on the efficacy of the action claimed. Because of their provisional nature, these descriptors will neither be revised nor included in the Cumulative Lists of INNs.

Dénominations communes internationales des Substances pharmaceutiques (DCI)

Il est notifié que, conformément aux dispositions de l'article 3 de la Procédure à suivre en vue du choix de Dénominations communes internationales recommandées pour les Substances pharmaceutiques les dénominations ci-dessous sont mises à l'étude par l'Organisation mondiale de la Santé en tant que dénominations communes internationales proposées. L'inclusion d'une dénomination dans les listes de DCI proposées n'implique aucune recommandation en vue de l'utilisation de la substance correspondante en médecine ou en pharmacie.

On trouvera d'autres listes de Dénominations communes internationales proposées (1-73) et recommandées (1-35) dans la *Liste récapitulative No. 9, 1996*. Les mentions indiquant les propriétés et les indications des substances sont fondées sur les renseignements communiqués par le fabricant. Elles ne visent qu'à donner une idée de l'utilisation potentielle des nouvelles substances au moment où elles sont l'objet de propositions de DCI. L'OMS n'est pas en mesure de confirmer ces déclarations ni de faire de commentaires sur l'efficacité du mode d'action ainsi décrit. En raison de leur caractère provisoire, ces informations ne figureront pas dans les listes récapitulatives de DCI.

Denominaciones Comunes Internacionales para las Sustancias Farmacéuticas (DCI)

De conformidad con lo que dispone el párrafo 3 del "Procedimiento de Selección de Denominaciones Comunes Internacionales Recomendadas para las Sustancias Farmacéuticas", se comunica por el presente anuncio que las denominaciones detalladas en las páginas siguientes están sometidas a estudio por la Organización Mundial de La Salud como Denominaciones Comunes Internacionales Propuestas. La inclusión de una denominación en las listas de las DCI Propuestas no supone recomendación alguna en favor del empleo de la sustancia respectiva en medicina o en farmacia.

Las listas de Denominaciones Comunes Internacionales Propuestas (1-73) y Recomendadas (1-35) se encuentran reunidas en *Cumulative List No. 9, 1996*. Las indicaciones sobre acción y uso que aparecen se basan principalmente en la información facilitada por los fabricantes. Esta información tiene por objeto dar una idea únicamente de las posibilidades de aplicación de las nuevas sustancias a las que se asigna una DCI Propuesta. La OMS no está facultada para respaldar esas indicaciones ni para formular comentarios sobre la eficacia de la acción que se atribuye al producto. Debido a su carácter provisional, esos datos descriptivos no deben incluirse en las listas recapitulativas de DCI.

Proposed International Nonproprietary Names: List 76

Comments on, or formal objections to, the proposed names may be forwarded by any person to the INN Programme of the World Health Organization within four months of the date of their publication in *WHO Drug Information*, i.e., for List 76 Proposed INN not later than 15 July 1997.

Dénominations communes internationales proposées: Liste 76

Des observations ou des objections formelles à l'égard des dénominations proposées peuvent être adressées par toute personne au Programme des Dénominations communes internationales de l'Organisation mondiale de la Santé dans un délai de quatre mois à compter de la date de leur publication dans *WHO Drug Information*, c'est à dire pour la Liste 76 de DCI Proposées le 15 juillet 1997 au plus tard.

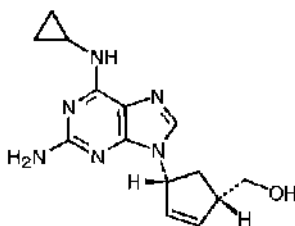
Denominaciones Comunes Internacionales Propuestas: Lista 76

Cualquier persona puede dirigir observaciones u objeciones respecto de las denominaciones propuestas, al Programa de Denominaciones Comunes Internacionales de la Organización Mundial de la Salud, en un plazo de cuatro meses, contados desde la fecha de su publicación en *WHO Drug Information*, es decir, para la Lista 76 de DCI Propuestas el 15 de julio de 1997 a más tardar.

<i>Proposed INN (Latin, English, French, Spanish)</i>	<i>Chemical name or description: Action and use: Molecular formula Chemical Abstracts Service (CAS) registry number: Graphic formula</i>
<i>DCI Proposée</i>	<i>Nom chimique ou description: Propriétés et indications. Formule brute Numéro dans le registre du CAS: Formule développée</i>
<i>DCI Propuesta</i>	<i>Nombre químico o descripción: Acción y uso: Fórmula empírica Número de registro del CAS: Fórmula desarrollada</i>

abacavirum

abacavir	(1 <i>S</i> ,4 <i>R</i>)-4-[2-amino-6-(cyclopropylamino)-9 <i>H</i> -purin-9-yl]-2-cyclopentene-1-methanol <i>antiviral</i>
abacavir	[(1 <i>S</i> ,4 <i>R</i>)-4-[2-amino-6-(cyclopropylamino)-9 <i>H</i> -purin-9-yl]cyclopent-2-ényl]méthanol <i>antiviral</i>
abacavir	(1 <i>S</i> ,4 <i>R</i>)-4-[2-amino-6-(ciclopropilamino)-9 <i>H</i> -purin-9-il]-2-ciclopenteno-1-metanol <i>antiviral</i>
	C ₁₄ H ₁₈ N ₆ O 136470-78-5



avitriptanum

avitriptan

3-[3-[4-(5-methoxy-4-pyrimidinyl)-1-piperazinyl]propyl]-*N*-methylindole-5-methanesulfonamide*antimigraïne, serotonin receptor agonist*

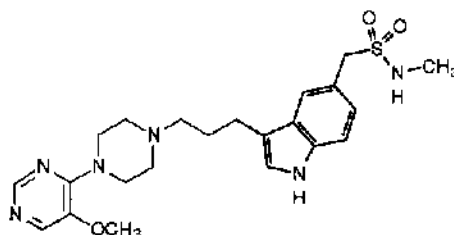
avitriptan

[3-[3-[4-(5-méthoxy-pyrimidin-4-yl)pipérazin-1-yl]propyl]-1*H*-indol-5-yl]-*N*-méthylméthanesulfonamide*antimigraïeux, agoniste des récepteurs de la sérotonine*

avitriptán

3-[3-[4-(5-metoxi-4-pirimidinil)-1-piperazinil]propil]-*N*-metilindol-5-metanosulfonamida*antimigrañoso, agonista de los receptores de la serotonina*C₂₂H₃₀N₆O₃S

151140-96-4

**balaperidonum**

balaperidone

(+)-3-[2-[(1*S*,5*R*,6*S*)-6-(*p*-fluorophenyl)-3-azabicyclo[3.2.0]hept-3-yl]ethyl]-2,4(1*H*,3*H*)-quinazolinédione*antipsychotic*

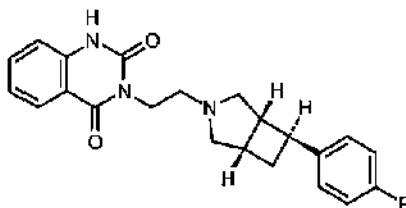
balapéridone

(+)-3-[2-[(1*S*,5*R*,6*S*)-6-(4-fluorophényl)-3-azabicyclo[3.2.0]hept-3-yl]éthyl]=quinazoline-2,4(1*H*,3*H*)-dione*psychotrope*

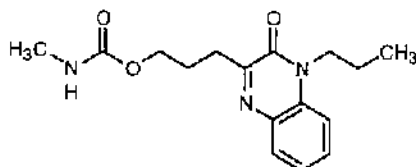
balaperidona

(+)-3-[2-[(1*S*,5*R*,6*S*)-6-(*p*-fluorofenil)-3-azabicyclo[3.2.0]hept-3-yl]etil]-2,4(1*H*,3*H*)-quinazolinadiona*antipsicótico*C₂₂H₂₂FN₃O₂

156862-51-0



bamaquimastum	
bamaquimast	3-(3-hydroxypropyl)-1-propyl-2(1 <i>H</i>)-quinoxalinone methylcarbamate (ester) <i>antiasthmatic</i>
bamaquimast	méthylcarbamate de 3-(3-oxo-4-propyl-3,4-dihydroquinoxalin-2-yl)propyle <i>antiasthmatique</i>
bamaquimast	metilcarbamato(éster) de 3-(3-hidroxipropil)-1-propil-2(1 <i>H</i>)-quinoxalinona <i>antiasmática</i>
	C ₁₆ H ₂₁ N ₃ O ₃ 135779-82-7

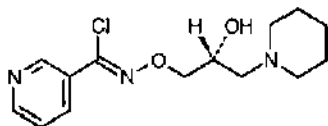


basiliximabum	
basiliximab	immunoglobulin G 1 (human-mouse monoclonal CH1621 heavy chain anti-human interleukin 2 receptor), disulfide with human-mouse monoclonal CH1621 light chain, dimer <i>immunomodulator</i>
basiliximab	immunoglobuline G 1 (chaîne lourde de l'anticorps monoclonal chimérique homme-souris CH1621 dirigé contre le récepteur humain de l'interleukine 2), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal chimérique homme-souris CH1621 <i>immunomodulateur</i>
basiliximab	immunoglobulina G 1 (cadena pesada del anticuerpo monoclonal quimérico hombre-ratón CH1621 dirigido contra el receptor humano de la interleuquina 2), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal quimérico hombre-ratón CH1621 <i>immunomodulador</i>
	179045-86-4

bimoclozolum	
bimoclozolol	(±)- <i>N</i> -(2-hydroxy-3-piperidinopropoxy)nicotinimidoylchloride <i>adjunctive antidiabetic agent</i>
bimoclozolol	chlorure de <i>N</i> -[(2 <i>RS</i>)-2-hydroxy-3-(pipéridin-1-yl)propoxy]pyridin-3-carboximidoyle <i>adjuvant d'antidiabétiques</i>
bimoclozolol	cloruro de (±)- <i>N</i> -(2-hidroxi-3-piperidinopropoxi)nicotinimidoyl <i>tratamiento coayudante en la diabetes</i>

C₁₄H₂₀ClN₃O₂

130493-03-7

and enantiomer
et l'enantiomère
y enantiómero**blonanserinum**

blonanserin

2-(4-ethyl-1-piperazinyl)-4-(*p*-fluorophenyl)-5,6,7,8,9,10-hexahydrocyclo=octa[*b*]pyridine
antipsychotic

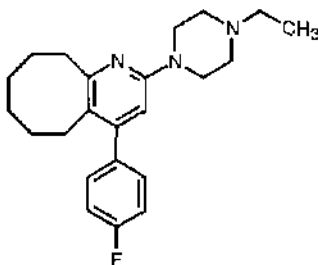
blonansérine

2-(4-éthylpipérazin-1-yl)-4-(4-fluorophényl)-5,6,7,8,9,10-hexahydrocyclo=octa[*b*]pyridine
psychotrope

blonanserina

2-(4-etil-1-piperazini)-4-(*p*-fluorofenil)-5,6,7,8,9,10-hexahidrociclo=octa[*b*]piridina
*antipsicótico*C₂₃H₃₀FN₃

132810-10-7

**brasofensinum**

brasofensine

3β-(3,4-dichlorophenyl)-1α,5αH-tropane-2α-carboxaldehyde
(*E*)-(O-methyloxime)
antiparkinsonian

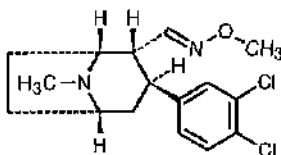
brasofensine

(1*R*,2*R*,3*S*,5*S*)-3-(3,4-dichlorophényl)-8-méthyl-8-azabicyclo[3.2.1]octane-2-carbaldehyde (*E*)-*O*-méthyloxime
antiparkinsonien

brasofensina

3β-(3,4-diclorofenil)-1αH,5αH-tropano-2α-carboxaldehído (*E*)-(O-metiloxima)
*antiparkinsoniano*C₁₆H₂₀Cl₂N₂O

171655-91-7



brinzolamidum

brinzolamide

(*R*)-4-(ethylamino)-3,4-dihydro-2-(3-methoxypropyl)-2*H*-thieno[3,2-*e*]-1,2-thiazine-6-sulfonamide 1,1-dioxide
carbonic anhydrase inhibitor

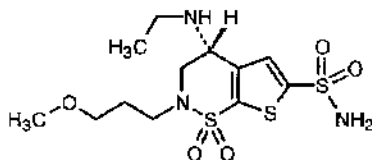
brinzolamide

(4*R*)-4-(éthylamino)-2-(3-méthoxypropyl)-3,4-dihydro-2*H*-thiéno[3,2-*e*]-1,2-thiazine-6-sulfonamide 1,1-dioxyde
inhibiteur de l'anhydrase carbonique

brinzolamida

(*R*)-4-(etilamino)-3,4-dihidro-2-(3-metoxipropil)-2*H*-tieno[3,2-*e*]-1,2-tiazina-6-sulfonamida 1,1-dióxido
inhibidor de la anhidrasa carbónica

C₁₂H₂₁N₃O₅S₃ 138890-62-7

**cevimelinum**

cevimeline

(±)-*cis*-2-methylspiro[1,3-oxathiolane-5,3'-quinuclidine]
nootropic agent

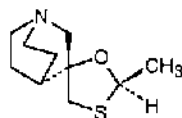
céviméline

(3*RS*,2'*RS*)-2'-méthylspiro[1-azabicyclo[2.2.2]octane-3,5'-(1,3)oxathiolane]
nootrope

cevimelina

(±)-*cis*-2-metilespiro[1,3-oxatiolano-5,3'-quinuclidina]
nootropo

C₁₀H₁₇NOS 107233-08-9



and enantiomer
et l'énantiomère
y enantiómero

cizolirtinum

cizolirtine

(±)-5-[α-[2-(dimethylamino)ethoxy]benzyl]-1-methylpyrazole
analgesic

cizolirtine

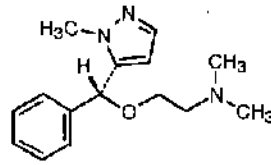
N,N-diméthyl-2-[(*RS*)-(1-méthyl-1*H*-pyrazol-5-yl)phénylméthoxy]éthylamine
analgésique

cizolirtina

(±)-5-[α-[2-(dimetilamino)etoxi]benzil]-1-metilpirazol
analgésico

C₁₅H₂₁N₃O

142155-43-9

and enantiomer
et l'énantiomère
y enantiómero**dalcotidinum**

dalcotidine

1-ethyl-3-[3-[(α -piperidino-*m*-tolyl)oxy]propyl]urea
antiulcer agent, histamine-H₂ receptor antagonist

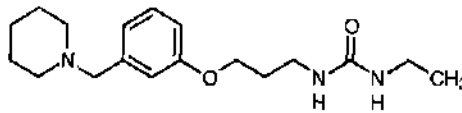
dalcotidine

1-éthyl-3-[3-[3-[(pipéridin-1-yl)méthyl]phénoxy]propyl]urée
antiulcéreux, antagoniste des récepteurs H₂ de l'histamine

dalcotidina

1-etil-3-[3-[(α -piperidino-*m*-tolil)oxi]propil]urea
*antiulcerosa, antagonista de los receptores H₂ de la histamina*C₁₈H₂₉N₃O₂

120958-90-9

**daniplestimum**

daniplestim

14-L-alanine-18-L-isoleucine-25-L-histidine-29-L-arginine-32-L-asparagine-
37-L-proline-42-L-serine-45-L-methionine-51-L-arginine-55-L-threonine-
59-L-leucine-62-L-valine-67-L-histidine-69-L-glutamic acid-73-glycine-
76-L-alanine-79-L-arginine-82-L-glutamine-87-L-serine-93-L-serine-
98-L-isoleucine-101-L-alanine-105-L-glutamine-109-L-glutamic acid-
116-L-valine-120-L-glutamine-123-L-glutamic acid-14-125-interleukin 3
(human clone D11 reduced)
immunomodulator

daniplestim

[14-L-alanine-18-L-isoleucine-25-L-histidine-29-L-arginine-32-L-asparagine-
37-L-proline-42-L-sérine-45-L-méthionine-51-L-arginine-55-L-thréonine-
59-L-leucine-62-L-valine-67-L-histidine-69-acide L-glutamique-73-glycine-
76-L-alanine-79-L-arginine-82-L-glutamine-87-L-sérine-93-L-sérine-
98-L-isoleucine-101-L-alanine-105-L-glutamine-109-acide L-glutamique-
116-L-valine-120-L-glutamine-123-acide L-glutamique]-14-125-interleukin 3
(clone humain D11 précurseur de la partie protéique réduite)
immunomodulateur

daniplestim

[14-L-alanina-18-L-isoleucina-25-L-histidina-29-L-arginina-32-L-asparagina-
37-L-prolina-42-L-serina-45-L-metionina-51-L-arginina-55-L-treonina-
59-L-leucine-62-L-valina-67-L-histidina-69-ácido L-glutámico-73-glicina-
76-L-alanina-79-L-arginina-82-L-glutamina-87-L-serina-93-L-serina-
98-L-isoleucina-101-L-alanina-105-L-glutamina-109-ácido L-glutámico-
116-L-valina-120-L-glutamina-123-ácido L-glutámico]-14-125-interleuquina 3
(clon humano D11 precursor de la fracción proteica reducida)
immunomodulador

C₅₆₄H₉₀₂N₁₈₁O₁₆₆S₅ 181753-30-6

ANCSTIMIDEI IHHLKRPPNF LLDPNNLNSE DMDILMERNL
 RTPNLLAFVR AVKHLENASG IEAILRNLQP CLPSATAAPS
 RHPIIIKAGD WQEFREKLTFF YLVTLEQAQE QQ

dexefaroxanum

dexefaroxan

(+)-(R)-2-(2-ethyl-2,3-dihydro-2-benzofuranyl)-2-imidazoline
α-adrenoreceptor antagonist

dexéfaroxan

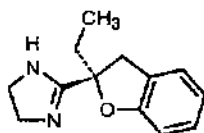
(+)-2-[(2R)-2-éthyl-2,3-dihydrobenzofuran-2-yl]-4,5-dihydro-1H-imidazole
antagoniste des récepteurs α-adrénérgiques

dexefaroxán

(+)-(R)-2-(2-etil-2,3-dihidro-2-benzofuranil)-2-imidazolina
antagonista de los receptores α-adrenérgicos

C₁₃H₁₆N₂O

143249-98-1

**elacridarum**

elacridar

4'-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl)ethyl]-5-methoxy-9-oxo-4-acridancarboxanilide
multidrug resistant inhibitor, antineoplastic

élaçridar

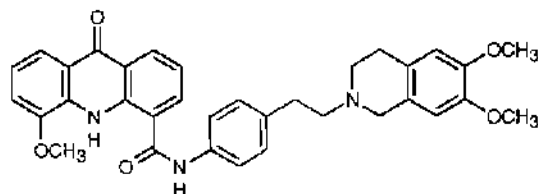
N-[4-(2-(6,7-diméthoxy-3,4-dihydroisoquinoléin-2(1H)-yl)éthyl)phényl]-5-méthoxy-9-oxo-9,10-dihydroacridine-4-carboxamide
inhibiteur de la multirésistance aux médicaments antinéoplasiques

elaçridar

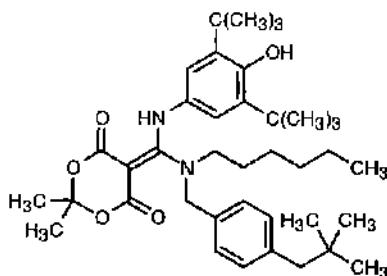
4'-[2-(3,4-dihidro-6,7-dimetoxi-2(1H)-isoquinolil)etil]-5-metoxi-9-oxo-4-acridancarboxanilida
Inhibidor de la resistencia a multiples fármacos antineoplásico

C₃₄H₃₃N₃O₅

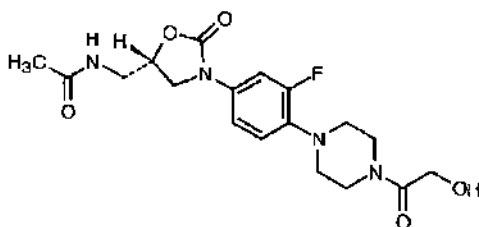
143664-11-3



eldacimibum	
eldacimibe	cyclic isopropylidene [(3,5-di- <i>tert</i> -butyl-4-hydroxyanilino)]hexyl=(<i>p</i> -neopentylbenzyl)amino)methylene]malonate <i>antihyperlipidaemic</i>
eldacimibe	5-[[[3,5-bis(1,1-diméthyléthyl)-4-hydroxyphényl]amino]]-[4-(2,2-diméthylpropyl)benzyl]hexylamino)méthylène]-2,2-diméthyl-1,3-dioxane-4,6-dione <i>antihyperlipémiant</i>
eldacimiba	[(3,5-di- <i>tert</i> -butyl-4-hydroxyanilino)]hexyl(<i>p</i> -neopentylbenzyl)amino)=méthylène]malonato cíclico de isopropilideno <i>antihiperlipémico</i>
	C ₃₉ H ₅₈ N ₂ O ₅ 141993-70-6



eperezolidum	
eperezolid	<i>N</i> -[[[(<i>S</i>)-3-[3-fluoro-4-(4-glycoloyl-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide <i>antibacterial</i>
épérezolide	<i>N</i> -[[[(<i>S</i>)-3-[3-fluoro-4-[4-(2-hydroxyacétyl)pipérazin-1-yl]phényl]-2-oxooxazolidin-5-yl]méthyl]acétamide <i>antibactérien</i>
eperezolida	<i>N</i> -[[[(<i>S</i>)-3-[3-fluoro-4-(4-glicololil-1-piperazinil)fenil]-2-oxo-5-oxazolidinil]metil]acetamida <i>antibacteriano</i>
	C ₁₈ H ₂₃ FN ₄ O ₅ 165800-04-4



esatenololum

esatenolol

2-[*p*-[(2*S*)-2-hydroxy-3-(isopropylamino)propoxy]phenyl]acetamide
β-adrenoceptor antagonist

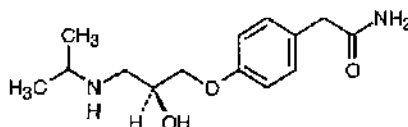
ésaténolol

2-[4-[(2*S*)-2-hydroxy-3-[(1-méthyléthyl)amino]propoxy]phényl]acétamide
antagonistes des récepteurs β-adrénergiques

esatenolol

2-[*p*-[(2*S*)-2-hidroxi-3-(isopropilamino)propoxi]fenil]acetamida
antagonista de los receptores β-adrenérgicosC₁₄H₂₂N₂O₃

93379-54-5

**faralimomabum**

faralimomab

Immunoglobulin G 1 (mouse monoclonal 64G12 γ 1-chain anti-human interferon receptor), disulfide with mouse monoclonal 64G12 light chain, dimer
immunomodulator

faralimomab

immunoglobuline G 1 (chaîne γ 1 de l'anticorps monoclonal de souris (64G12) dirigé contre le récepteur humain des interférons de type I), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de souris 64G12*immunomodulateur*

faralimomab

inmunoglobulina G 1 (cadena γ 1 del anticuerpo monoclonal de ratón (64G12) dirigida contra el receptor humano de los interferones de tipo I), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal de ratón 64G12*immunomodulador*

167816-91-3

gacyclidinum

gacyclidine

1-[*cis*-2-methyl-1-(2-thienyl)cyclohexyl]piperidine
NMDA receptor antagonist

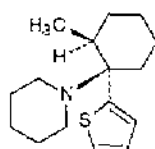
gacyclidine

1-[(1*RS*,2*SR*)-2-méthyl-1-(thiophén-2-yl)cyclohexyl]pipéridine
antagoniste des récepteurs du NMDA

gacyclidina

1-[*cis*-2-metil-1-(2-tienil)ciclohexil]piperidina
*antagonista de los receptores de NMDA*C₁₆H₂₃NS

68134-81-6

and enantiomer
et l'énantiomère
y enantiómero

ganaxolonum

ganaxolone

3 α -hydroxy-3-methyl-5 α -pregnan-20-one
anticonvulsant

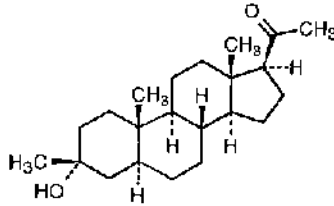
ganaxolone

3 α -hydroxy-3-méthyl-5 α -prégnan-20-one
anticonvulsivant

ganaxolona

3 α -hidroxi-3-metil-5 α -pregnan-20-ona
*anticonvulsivo*C₂₂H₃₈O₂

38398-32-2

**hemoglobinum crosfumarilum**

hemoglobín crosfumaril

hemoglobin A₀ (human $\alpha_2\beta_2$ tetrameric subunit), α -chain 99,99'-diamide with fumaric acid
hemoglobin derivative

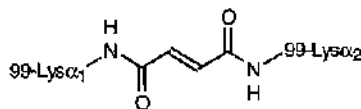
hémoglobine crosfumaril

99,99'-diamide de la chaîne α de l'hémoglobine A₀ (sous-unité tétramérique $\alpha_2\beta_2$ humaine) avec l'acide fumarique
dérivé de l'hémoglobine

hemoglobina crosfumarilo

99,99'-diamida de la cadena α de la hemoglobina A₀ (subunidad tetramérica $\alpha_2\beta_2$ humana), con el ácido fumárico
derivado de hemoglobina

142261-03-8

**indisetrinum**

indisetrón

N-(3,9-dimethyl-endo-3,9-diazabicyclo[3.3.1]non-7-yl)-1*H*-indazole-3-carboxamide
serotonin receptor antagonist

indisétron

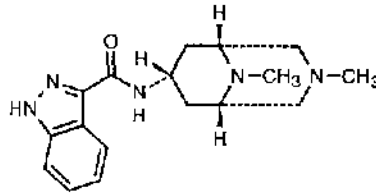
N-[(1*R*,5*S*,7*S*)-3,9-diméthyl-3,9-diazabicyclo[3.3.1]non-7-yl]-1*H*-indazole-3-carboxamide
antagoniste de récepteurs de la sérotonine

indisetrón

N-(3,9-dimetil-endo-3,9-diazabicyclo[3.3.1]non-7-il)-1*H*-indazol-3-carboxamida
antagonista de los receptores de la serotonina

C₁₇H₂₉N₅O

141549-75-9

**insulinum aspartum**

insulin aspart

28^B-L-aspartic acid-insulin (human)
antidiabetic

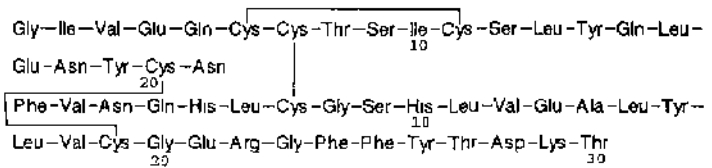
insuline asparte

[28^B-acide L-aspartique]insuline humaine
antidiabétique

insulina asparta

28^B-L-ácido aspártico-insulina(humana)
*antidiabético*C₂₅₆H₃₈₁N₆₅O₇₉S₆

116094-23-6

**insulinum glarginum**

insulin glargine

21^A-glycine-30^{Ba}-L-arginine-30^{Bb}-L-arginineinsulin (human)
antidiabetic

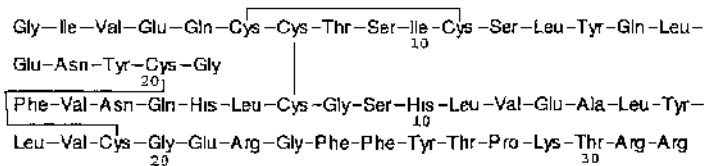
insuline glargine

[21^A-glycine]30^{Ba}-L-arginine-30^{Bb}-L-arginine-insuline humaine
antidiabétique

insulina glargina

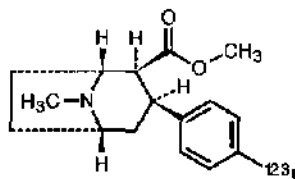
21^A-glicina-30^{Ba}-L-arginina-30^{Bb}-L-argininainsulina (humana)
*antidiabético*C₂₈₇H₄₀₄N₇₂O₇₈S₆

160337-95-1



iometopanum (¹²³I)iometopane (¹²³I)methyl 3β-(*p*-[¹²³I]iodophenyl)-1α,5α-tropane-2β-carboxylate
*diagnostic agent*iométopane (¹²³I)(1*R*,2*S*,3*S*,5*S*)-3-(4-[¹²³I]iodophényl)-8-méthyl-8-azabicyclo[3.2.1]octane-2-carboxylate de méthyle
*produit à usage diagnostique*iometopano (¹²³I)3β-(*p*-[¹²³I]iodofenil)-1α,5α-tropano-2β-carboxilato de metilo
*agente de diagnóstico*C₁₆H₂₀¹²³INO₂

136794-86-0

**israpafantum**

israpafant

(±)-4-(*o*-chlorophenyl)-2-(*p*-isobutylphenethyl)-6,9-dimethyl-6*H*-thieno[3,2-*f*]-s-triazolo[4,3-*a*][1,4]diazepine
platelet activating factor antagonist

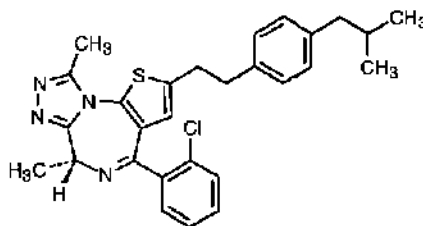
israpafant

(6*RS*)-4-(2-chlorophényl)-6,9-diméthyl-2-[2-[4-(2-méthylpropyl)phényl]éthyl]-6*H*-thiéo[3,2-*f*][1,2,4]triazolo[4,3-*a*][1,4]diazépine
antagoniste du facteur activant les plaquettes

israpafant

(±)-4-(*o*-chlorofenil)-2-(*p*-isobutilfenetil)-6,9-dimetil-6*H*-tieno[3,2-*f*]-s-triazolo[4,3-*a*][1,4]diazepina
*antagonista del factor de activación de plaquetas*C₂₈H₂₉ClN₄S

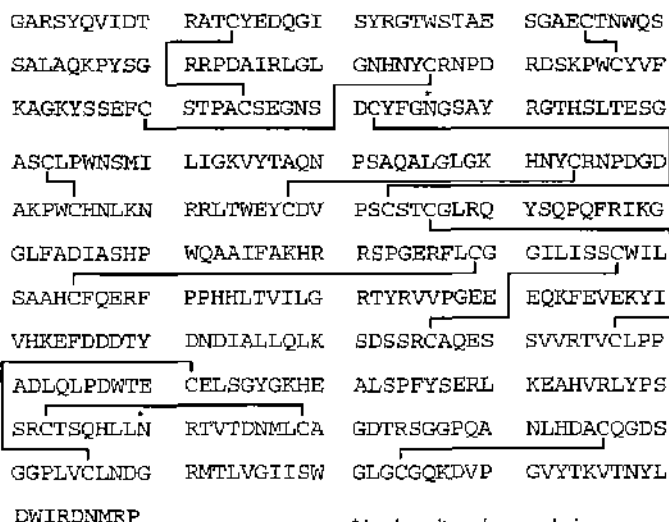
117279-73-9

and enantiomer
et énantiomère
y enantiómero**keliximabum**

keliximab

immunoglobulin G 1 (human-Macaca monoclonal CE9.1 γ1-chain anti-human antigen CD 4), disulfide with human-Macaca monoclonal CE9.1 κ-chain,
dimer
immunomodulator

kéliximab	immunoglobuline G 1 (chaîne γ 1 de l'anticorps monoclonal chimérique homme-macaque CE9.1 dirigé contre l'antigène CD 4 humain), dimère du disulfure avec la chaîne κ de l'anticorps monoclonal chimérique homme-macaque CE9.1 <i>immunomodulateur</i>
keliximab	immunoglobulina G 1 (cadena γ 1 del anticuerpo monoclonal quimérico hombre-macaco CE9.1 dirigido contra el antígeno CD4 humano), dímero del disulfuro con la cadena κ del anticuerpo monoclonal dimérico hombre-macaco CE9.1 <i>immunomodulador</i>
	174722-30-6
lanotepasum	
lanotéplase	<i>N</i> -[<i>N</i> ² -(<i>N</i> -glycyl-L-alanyl)-L-arginyl]-117-L-glutamine-245-L-methionine-(1-5)-(87-527)-plasminogen activator (human tissue-type protein moiety) <i>fibrinolytic</i>
lanotéplase	<i>N</i> -[<i>N</i> ² -(<i>N</i> -glycyl-L-alanyl)-L-arginyl]-[117-L-glutamine-245-L-méthionine]- (1-5)-(87-527)- activateur du plasminogène (type tissulaire humain, partie protéique) <i>thrombolytique</i>
lanotéplasa	<i>N</i> -[<i>N</i> ² -(<i>N</i> -glicil-L-alanil)-L-arginil]-[117-L-glutamina-245-L-metionina]- (1-5)-(87-527)-activador del plasminógeno (tipo tisular humano, fracción proteica) <i>trombolítico</i>
	C ₂₁₈₄ H ₃₃₂₃ N ₆₃₃ O ₆₆₆ S ₂₉ 171870-23-8



* binding sites of sugar chain

* sites de fixation de la chaîne osidique

* lugares de unión de la cadena osídica

lasinavirum

lasinavir

tert-butyl [(α S)- α -[(1S,3R)-1-hydroxy-3-[[[(1S)-1-(2-methoxyethyl)carbamoyl]-2-methylpropyl]carbamoyl]-4-(2,3,4-trimethoxyphenyl)butyl]phenethyl]=
carbamate
antiviral

lasinavir

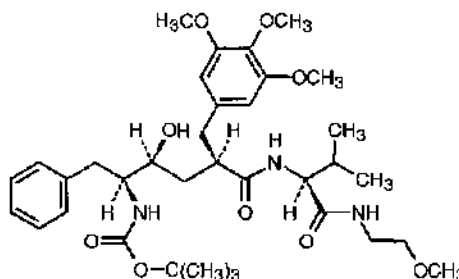
[(1S,2S,4R)-1-benzyl-2-hydroxy-5-[[[(1S)-1-(2-méthoxyéthyl)carbamoyl]-2-méthylpropyl]amino]-5-oxo-4-(3,4,5-triméthoxybenzyl)pentyl]carbamate de
1,1-diméthyléthyle
antiviral

lasinavir

[(α S)- α -[(1S,3R)-1-hidroxil-3-[[[(1S)-1-(2-metoxietil)-carbamoil]-2-metilpropil]carbamoil]-4-(2,3,4-trimetoxifenil)butil]fenetil]carbamato de *terc*-
butilo
antiviral

C₃₅H₅₃N₃O₉

175385-62-3

**ledoxantroneum**

ledoxantrone

5-[(2-aminoethyl)amino]-2-[2-(diethylamino)ethyl]-2H-[1]benzothioopyrano=
[4,3,2-*cd*]indazol-8-ol
antineoplástico

ledoxantrone

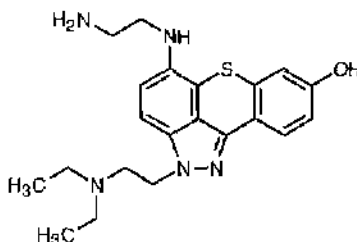
5-[(2-aminoéthyl)amino]-2-[2-(diéthylamino)éthyl]-2H-[1]benzothioopyrano=
4,3,2-*cd*]indazol-8-ol
antinéoplasique

ledoxantrona

5-[(2-aminoetil)amino]-2-[2-(dietilamino)etil]-2H-[1]benzotioopirano=
[4,3,2-*cd*]indazol-8-ol
antineoplásico

C₂₁H₂₇N₅OS

113457-05-9



linezolidum

linezolid

N-[[[(*S*)-3-(3-fluoro-4-morpholinophenyl)-2-oxo-5-oxazolidinyl]methyl]acetamide
antibacterial

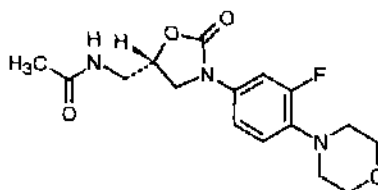
linézolide

N-[[[(*S*)-3-[3-fluoro-4-(morpholin-4-yl)phényl]-2-oxooxazolidin-5-yl]méthyl]acétamide
antibactérien

linezolid

N-[[[(*S*)-3-(3-fluoro-4-morfolinofenil)-2-oxo-5-oxazolidinil]metil]acetamida
antibacteriano

C₁₆H₂₀FN₃O₄ 165800-03-3

**lintuzumabum**

lintuzumab

immunoglobulin G 1 (human-mouse monoclonal HuM195 γ 1-chain anti-human antigen CD 33), disulfide with human monoclonal HuM195 κ -chain, dimer
immunomodulator

lintuzumab

immunoglobuline G 1 (chaîne légère γ 1 de l'anticorps monoclonal de souris humanisé HuM195 dirigé contre l'antigène CD 33 humain), dimère du disulfure avec la chaîne κ de l'anticorps monoclonal humain HuM195
immunomodulateur

lintuzumab

inmunoglobulina G 1 (cadena ligera γ 1 del anticuerpo monoclonal de ratón humanizado HuM195 dirigido contra el antígeno CD 33 humano), dímero del disulfuro con la cadena κ del anticuerpo monoclonal humano Hu195
immunomodulador

166089-32-3

metesindum

metesind

4-[[α -[(2-aminobenz[*cd*]indol-6-yl)methylamino]-*p*-tolyl]sulfonyl]morpholine
antineoplastic

métésind

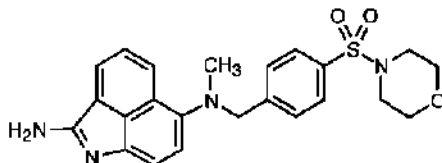
4-[[4-[[[(2-aminobenz[*cd*]indol-6-yl)(méthyl)amino]méthyl]phényl]=sulfonyl]morpholine
antineoplasique

metesind

4-[[α -[(2-aminobenz[*cd*]indol-6-il)metilamino]-*p*-tolil]sulfonyl]morfolina
antineoplásico

C₂₃H₂₄N₄O₃S

138384-68-6

**milfasartanum**

milfasartan

methyl 2-[[4-butyl-2-methyl-6-oxo-5-[*p*-(*o*-1*H*-tetrazol-5-yl)phenyl]benzyl]-1(6*H*)-pyrimidinyl]methyl]-3-thiophenecarboxylate
angiotensin II receptor antagonist

milfasartan

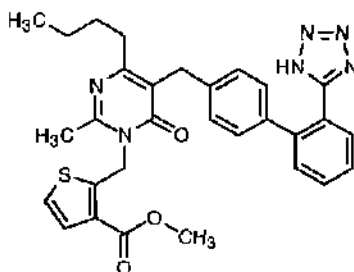
2-[[4-butyl-2-méthyl-6-oxo-5-[4-[2-(1*H*-tétrazol-5-yl)phényl]bénzyl]pyrimidin-1(6*H*)-yl]méthyl]thiophène-3-carboxylate de méthyle
antagoniste du récepteur de l'angiotensine II

milfasartán

2-[[4-butíl-2-metil-6-oxo-5-[*p*-(*o*-1*H*-tetrazol-5-ilfenil)]bencil]-1(6*H*)-pirimidinil]metil]-3-tiofenocarboxilato de metilo
antagonista del receptor de angiotensina II

C₃₀H₃₀N₈O₃S

148564-47-0

**minalrestatum**

minalrestat

(±)-2-(4-bromo-2-fluorobenzyl)-6-fluorospiro[isoquinoline-4(1*H*), 3'-pyrrolidine]-1,2',3,5'(2*H*)-tetrone
aldose reductase inhibitor

minalrestat

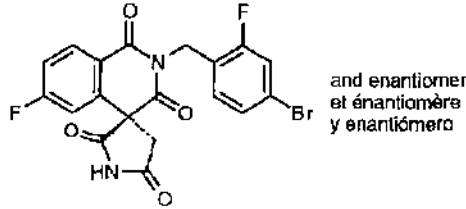
(3'*RS*)-2-(4-bromo-2-fluorobenzyl)-6-fluorospiro[isoquinoléine-4(1*H*), 3'-pyrrolidine]-1,2',3,5'(2*H*)-tétrone
inhibiteur de l'aldose réductase

minalrestat

(±)-2-(4-bromo-2-fluorobencil)-6-fluoroesp[iro]isoquinolina-4(1*H*), 3'-pirrolidin]-1,2',3,5'(2*H*)-tetrona
inhibidor de la aldose reductasa

C₁₉H₁₁BrF₂N₂O₄

129688-50-2



nagrestipenum
nagrestipen

26-L-alanine]ymphokine MIP 1 α (human clone pAT464 macrophage inflammatory)
immunomodulator

nagrestipen

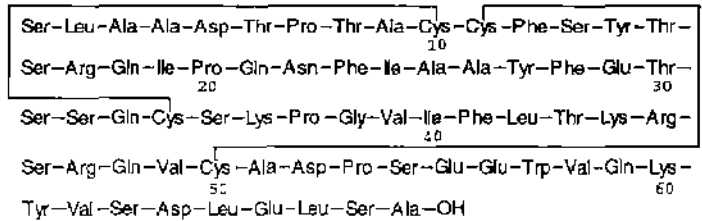
[26-L-alanine]ymphokine MIP 1 α (clone pAT464 de macrophage inflammatoire humain)
immunomodulateur

nagrestipen

[26-L-alanina]infoquina MIP 1 α (clon pAT464 de macrófago inflamatorio humano)
immunomodulador

C₃₂₈H₅₁₆N₈O₁₀₈S₄

166089-33-4



nelfinavirum
nelfinavir

(3*S*,4*aS*,8*aS*)-*N*-*tert*-butyl-2-[(2*R*,3*R*)-3-(3,2-cresotamido)-2-hydroxy-4-(phenylthio)butyl]decahydro-3-isoquinolinecarboxamide
antiviral

nelfinavir

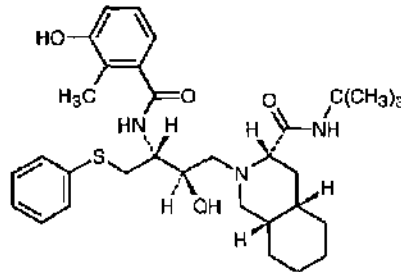
(3*S*,4*aS*,8*aS*)-*N*-(1,1-diméthyléthyl)-2-[(2*R*,3*R*)-2-hydroxy-3-[(3-hydroxy-2-méthylbenzoyl)amino]-4-(phénylsulfanyl)butyl]décahydroisoquinoléine-3-carboxamide
antiviral

nelfinavir

(3*S*,4*aS*,8*aS*)-*N*-*terc*-butil-2-[(2*R*,3*R*)-3-(3,2-cresotamido)-2-hidroxi-4-feniltio]butil]decahidro-3-isoquinolinacarboxamida
antiviral

C₃₂H₄₅N₃O₄S

159989-64-7



nerelimomabum
nerelimomab

immunoglobulin G 1 (mouse monoclonal BAYX1351 γ 1-chain anti-human tumor necrosis factor α), disulfide with mouse monoclonal BAYX1351 light chain, dimer
immunomodulator

nérélimomab

immunoglobuline G 1 (chaîne γ 1 de l'anticorps monoclonal de souris BAYX1351 dirigé contre le facteur de nécrose tumorale α humain), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de souris BAYX1351
immunomodulateur

nerelimomab

immunoglobulina G 1 (cadena ligera mouse monoclonal BAYX1351 γ 1-chain anti-human tumor necrosis factor α), disulfide with mouse monoclonal BAYX1351 light chain, dimer
immunomodulador

162774-06-3

omiloxetinum
omiloxetine

4'-fluoro-2-[*trans*-4-(*p*-fluorophenyl)-3-[[3,4-(methylenedioxy)=phenoxy]methyl]piperidino]acetophenone
antidepressant

omiloxétine

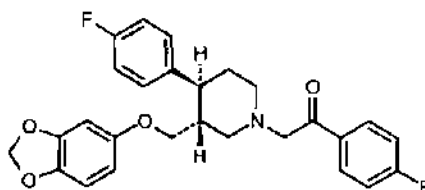
2-[(3*RS*,4*SR*)-3-[(1,3-benzodioxol-5-yloxy)méthyl]-4-(4-fluorophényl)=pipéridin-1-yl]-1-(4-fluorophényl)éthanone
antidépresseur

omiloxetino

4'-fluoro-2-[*trans*-4-(*p*-fluorofenil)-3-[[3,4-(metilenedioxi)=fenoxi]metil]piperidino]acetofenona
antidepressivo

C₂₇H₂₅F₂NO₄

176894-09-0



and enantiomer
et l'énantiomère
y enantiómero

opratonil iodidum
opratonium iodide

trimethyl[3-(undecenamido)propyl]ammonium iodide
antiseptic

iodure d'opratonium

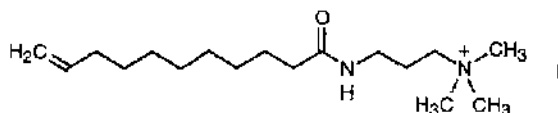
iodure de *N,N,N*-triméthyl-3-(undéc-10-énoylamino)propan-1-aminium
antiseptique

ioduro de opratonio

ioduro de trimetil[3-(undecenamido)propil]amonio
antiséptico

$C_{17}H_{35}N_2O$

146913-78-0



oprelvekinum
oprelvekin

2-178-interleukin 11 (human clone pXM/IL-11)
immunomodulator

oprelvékine

2-178-interleukine 11 (clone humain pXM/IL-11)
immunomodulateur

oprelvekina

2-178-interleuquina 11 (clon humano pXM/IL-11)
immunomodulador

$C_{654}H_{1411}N_{253}O_{235}S_2$

145941-26-0

GPPPGPPRVS PDPRAEIDST VLLTRSLAD TRQLAAQLRD
KFPADGDHNL DSLPTLAMS GALGALQLPG VLTRLRADLL
SYLRHVQWLR RAGGSSLKTL EPGLGTQAR LDRLLRLQL
LMSRLALPQP PPDPAPPPLA PPSSAWGGIR AAHAILGGLH
LTLDWAVRGL LLLKTRL

osutidinum
osutidine

(±)-N-[(E)-{(p,β-dihydroxyphenethyl)amino}][2-[[5-[(methylamino)=methyl]furfuryl]thio]ethyl]amino]methylene]methanesulfonamide
histamine-H₂ receptor antagonist

osutidine

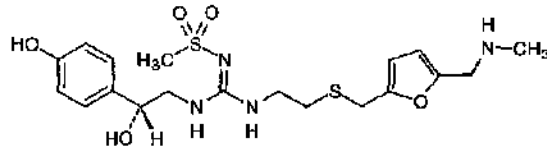
(E)-1-[(2RS)-2-hydroxy-2-(4-hydroxyphényl)éthyl]-3-[2-[[5-[(méthylamino)=méthyl]-2-furyl]méthyl]sulfa(nyl)éthyl]-2-(méthylsulfonyl)guanidine
antagoniste des récepteurs H₂ de l'histamine

osutidina

(±)-N-[(E)-{(p,β-dihidroxiifenetil)amino}][2-[[5-[(metilamino)=metil]furfuril]tio]etil]amino]metileno]metanosulfonamida
antagonista de los receptores H₂ de la histamina

C₁₉H₂₈N₄O₅S₂

140695-21-2



and enantiomer
et l'énantiomère
y enantiomero

pelubiprofenum
pelubiprofen

(±)-p-[(E)-2-oxocyclohexylidene]methyl]hydatropic acid
non-steroidal anti-inflammatory

pélubiprofène

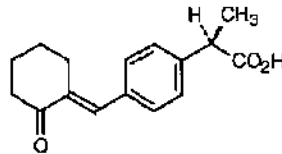
acide (2RS)-2-[4-[(E)-2-oxocyclohexylidène)méthyl]phényl]propanoïque
anti-inflammatoire non-stéroïdien

pelubiprofeno

ácido(±)-p-[(E)-2-oxociclohexiliden]metil]hidratrópico
antiinflamatorio no esteroideo

C₁₆H₁₈O₃

69956-77-0



and enantiomer
et énantiomère
y enantiómero

pumaprazolum
pumaprazole

methyl 2-[(2,3-dimethylimidazo[1,2-a]pyridin-8-yl)amino]methyl]-3-methylcarbamilate
antiulcer agent

pumaprazole

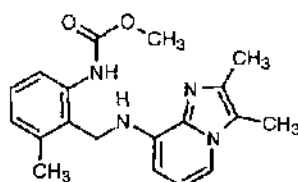
2-[(2,3-diméthylimidazo[1,2-a]pyridin-8-yl)amino]méthyl]-3-méthylphényl]carbamate de méthyle
antifucéreux

pumaprazol

2-[(2,3-dimetilimidazo[1,2-a]piridin-8-il)amino]metil]-3-metilcarbanilato de metilo
antiulceroso

C₁₉H₂₂N₄O₂

158364-59-1

**quilostigminum**

quilostigmine

(3a*S*,8a*R*)-1,2,3,3a,8,8a-hexahydro-1,3a,8-triméthylpyrrolo[2,3-*b*]indol-5-yl 3,4-dihydro-2(1*H*)-isoquinolinecarboxylate
acétylcholinestérase inhibiteur

quilostigmine

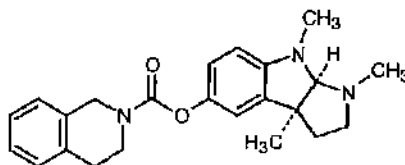
3,4-dihydroisoquinoléine-2(1*H*)-carboxylate de (3a*S*,8a*R*)-1,3a,8-triméthyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indol-5-yle
inhibiteur de l'acétylcholinestérase

quilostigmina

3,4-dihidro-2(1*H*)-isoquinolinacarboxilato de (3a*S*,8a*R*)-1,2,3,3a,8,8a-hexahidro-1,3a,8-trimetilpirrolo[2,3-*b*]indol-5-ilo
inhibidor de la acetilcolinesterasa

C₂₃H₂₇N₃O₂

139314-01-5

**retigabinum**

retigabine

ethyl 2-amino-4-[(*p*-fluorobenzyl)amino]carbanilate
anticonvulsant, antiepileptic

rétigabine

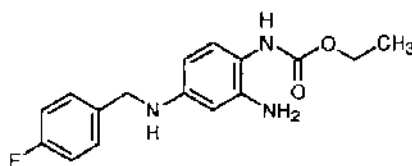
[2-amino-4-[(4-fluorobenzyl)amino]phényl]carbamate d'éthyle
anticonvulsivant, antiépileptique

retigabina

2-amino-4-[(*p*-fluorobencil)amino]carbanilato de etilo
anticonvulsivo, antiépileptico

C₁₆H₁₃FN₃O₂

150812-12-7



sabcomelinum

sabcomeline

(R)-3-quinuclidineglyoxylonitrile (*Z*)-(*O*)-methyloxime
nootropic agent

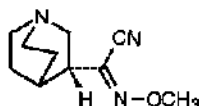
sabcoméline

(Z)-2-[(3*R*)-1-azabicyclo[2.2.2]oct-3-yl]-2-(méthoxyimino)acétonitrile
nootrope

sabcomelina

(R)-3-quinuclidinagloxilonitrilo (*Z*)-(*O*)-metiloxima
*nootropo*C₁₀H₁₅N₃O

159912-53-5

**scopinastum**

scopinast

7-[3-[4-[bis(*p*-fluorophenyl)hydroxymethyl]piperidino]propoxy]-
6-methoxycoumarin
antiallergic, antiasthmatic

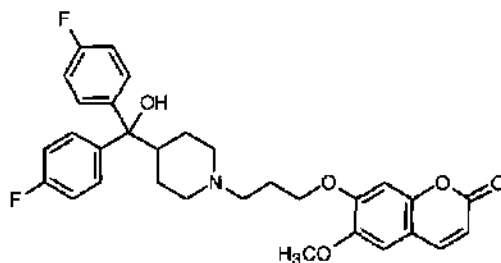
scopinast

7-[3-[4-[bis(4-fluorophényl)hydroxyméthyl]pipéridin-1-yl]propoxy]-6-méthoxy-
2*H*-chromén-2-one
antiallergique, antiasthmatique

escopinast

7-[3-[4-[bis(*p*-fluorofenil)hidroximetil]piperidino]propoxi]-6-metoxicumarina
*antialérgico, antiasmático*C₃₁H₃₁F₂NO₅

145574-90-9

**soretolidum**

soretolide

2,6-dimethyl-*N*-(5-methyl-3-isoxazolyl)benzamide
anticonvulsant

sorétolide

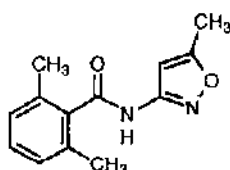
2,6-diméthyl-*N*-(5-méthylisoxazol-3-yl)benzamide
anticonvulsivant

soretolida

2,6-dimetil-*N*-(5-metil-3-isoxazoli)benzamida
anticonvulsivo

C₁₃H₁₄N₂O₂

130403-08-6

**tasonerminum**

tasonermin

1-157-tumor necrosis factor alfa-1a (human)
antineoplastico

tasonemine

1-157-facteur de nécrose tumorale humain alfa-1a
antineoplasique

tasonermina

1-157-factor de necrosis tumoral alfa-1a (humano)
*antineoplásico*C₇₇₈H₁₂₂₅N₂₁₅O₂₃₁S₂ 94948-59-1

VRSSSRTPSD KPAHVVANP QAEGQLQWLN RRANALLANG
VELRDNQLVV PSEGLYLIYS QVLFKQGQCP STHVLLTHTI
SRIAVSYQTK VMLLSAIKSP CQRETPEGAE AKPWYEPIYL
GGVFQLEKGD RLSAEINRPD YLDFAESGQV YFGIIAL

technetium (^{99m}Tc) nofetumomabum

merpentanum

technetium (^{99m}Tc) nofetumomab

merpentan

immunoglobulin G 2b (mouse monoclonal NR-LU-10 Fab fragment anti-human tumor), disulfide with mouse monoclonal NR-LU-10 x-chain, [N,N'-[(2-formylethyl)ethylene]bis[2-mercaptoacetamido]]= (4-)-N,N',S,S']oxo[^{99m}Tc]technetate(1-) conjugate
radiodiagnostic agent

technétium (^{99m}Tc) nofétumomab

merpentan

immunoglobuline G 2b (fragment Fab de l'anticorps monoclonal de souris NR-LU-10 dirigé contre une tumeur humaine), disulfure avec la chaîne x de l'anticorps monoclonal de souris NR-LU-10 conjuguée avec l'oxo-[[N,N'-[1-(3-oxopropyl)éthane-1,2-diy]]bis[2-sulfanylacétamido]](4-)-N,N',S,S'] = [^{99m}Tc]technétate(1-)
produit a usage radiodiagnostique

tecnecio (^{99m}Tc) nofetumomab

merpentán

immunoglobulina G 2b (fragmento Fab del anticuerpo monoclonal de ratón NR-LU-10 dirigido contra un tumor humano), disulfuro con la cadena x del anticuerpo monoclonal de ratón NR-LU-10 conjugado con el oxo-[[N,N'-[1-(3-oxopropil)etano-1,2-dil]]bis[2-sulfanilacetamido]] = (4-)-N,N',S,S'] [^{99m}Tc]tecnecato(1-)
agente de radiodiagnóstico

165942-79-0

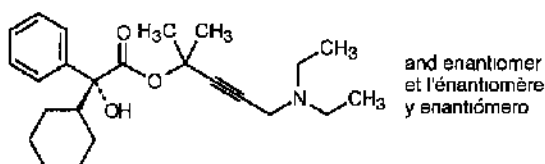
temiverinum

temiverine 4-(diethylamino)-1,1-dimethyl-2-butynyl (±)- α -phenylcyclohexaneglycolate
antispasmodic

témivérine (2*RS*)-2-cyclohexyl-2-hydroxy-2-phénylacétate de 4-(diéthylamino)-1,1-diméthylbut-2-ynyle
antispasmodique

temiverina (±)- α -fenilciclohexanoglicolato de 4-(dielilamino)-1,1-dimetil-2-butinilo
antiespasmódico

$C_{24}H_{35}NO_3$ 173324-94-2

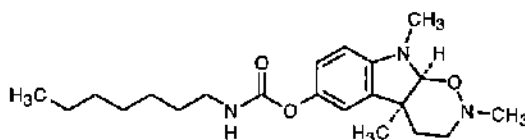
**t eserstiginum**

t eserstigmine (4*aS*,9*aS*)-2,3,4,4*a*,9,9*a*-hexahydro-2,4*a*,9-trimethyl-1,2-oxazino[6,5-*b*]indol-6-yl heptylcarbamate
nootropic agent

téserstigmine heptylcarbamate de (4*aS*,9*aS*)-2,4*a*,9-triméthyl-2,3,4,4*a*,9,9*a*-hexahydro-1,2-oxazino[6,5-*b*]indol-6-yle
nootrope

t eserstigmina heptilcarbamato de (4*aS*,9*aS*)-2,3,4,4*a*,9,9*a*-hexahidro-2,4*a*,9-trimetil-1,2-oxazino[6,5-*b*]indol-6-ilo
nootropo

$C_{21}H_{33}N_3O_3$ 147650-57-5

**ticolubantum**

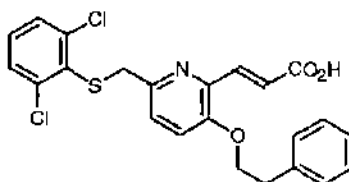
ticolubant (*E*)-6-[[[(2,6-dichlorophenyl)thio]methyl]-3-(phenethoxy)-2-pyridineacrylic acid
leukotriene receptor antagonist

ticolubant acide (*E*)-3-[6-[[[(2,6-dichlorophényl)sulfanyl]méthyl]-3-(2-phényléthoxy)=pyridin-2-yl]prop-2-énoïque
antagoniste du récepteur des leucotriènes

ticolubant ácido (*E*)-6-[[[(2,6-diclorofenil)tio]metil]-3-(fenetiloxi)-2-piridinacrílico
antagonista del receptor de leucotrienos

C₂₃H₁₉Cl₂NO₃S

154413-61-3

**valsopodarum**

valsopodar

cyclo[[*(2S,4R,6E)*-4-méthyl-2-(méthylamino)-3-oxo-6-octénoyl]-L-valyl-*N*-méthylglycyl-*N*-méthyl-L-leucyl-L-valyl-*N*-méthyl-L-leucyl-*D*-alanyl-*D*-alanyl-*N*-méthyl-L-leucyl-*N*-méthyl-L-leucyl-*N*-méthyl-L-valyl]
multidrug resistant inhibitor, antineoplastic

valsopodar

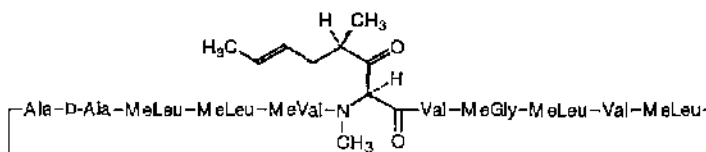
cyclo[L-alanyl-*D*-alanyl-*N*-méthyl-L-leucyl-*N*-méthyl-L-leucyl-*N*-méthyl-L-valyl-[[*(2S,4R,6E)*-4-méthyl-2-(méthylamino)-3-oxooct-6-énoyl]-L-valyl-*N*-méthylglycyl-*N*-méthyl-L-leucyl-L-valyl-*N*-méthyl-L-leucyl]
inhibiteur de la multirésistance aux médicaments antinéoplasiques

valsopodar

ciclo[[*(2S,4R,6E)*-4-metil-2-(metilamino)-3-oxo-6-octenoil]-L-valil-*N*-metilglicil-*N*-metil-L-leucil-L-valil-*N*-metil-L-leucil-L-alanil-*D*-alanil-*N*-metil-L-leucil-*N*-metil-L-leucil-*N*-metil-L-valil]
inhibidor de la resistencia a multiples fármacos antineoplásico

C₆₃H₁₁₁N₁₁O₁₂

121584-18-7

**vedaclidinum**

vedaclidine

(*S*)-3-[4-(butylthio)-1,2,5-thiadiazol-3-yl]quinuclidine
analgesic

vedaclidine

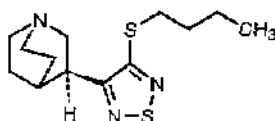
(*S*)-3-[4-(butylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azabicyclo[2.2.2]octane
analgésique

vedaclidina

(*S*)-3-[4-(butiltio)-1,2,5-tiadiazol-3-il]quinuclidina
analgésico

C₁₃H₂₁N₃S₂

141575-50-0



Names for Radicals and Groups

Some substances for which an international nonproprietary name has been established may be used in the form of salts or esters. The radicals or groups involved may be of complex composition and it is then inconvenient to refer to them in systematic chemical nomenclature. Consequently, shorter nonproprietary names for some radicals and groups have been devised or selected, and they are suggested for use with the proposed and recommended international nonproprietary names

Dénominations applicables aux radicaux et groupes

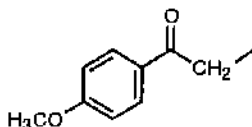
Certaines substances pour lesquelles une dénomination commune internationale a été établie sont parfois utilisées sous forme de sels ou d'esters. Les radicaux ou groupes correspondants sont alors quelquefois si complexes qu'il est malcommode de les désigner conformément à la nomenclature chimique systématique. Des dénominations communes abrégées ont donc été formées ou choisies pour certains d'entre eux et ils est suggéré de les employer avec les dénominations communes internationales proposées et recommandées.

Denominaciones para Radicales y Grupos

Ciertas sustancias para las cuales hay establecida una denominación común pueden usarse en forma de sales o de ésteres. Los radicales o grupos correspondientes pueden llegar a tener una composición tan compleja que resulte incómodo referirse a ellos mediante la nomenclatura química sistemática. Las siguientes denominaciones comunes abreviadas han sido ideadas o elegidas para algunos de estos radicales y grupos y se sugiere que se empleen con las denominaciones comunes internacionales propuestas y recomendadas

anisatflum

anisatil	2-(4-methoxyphenyl)-2-oxoethyl
anisatil	2-(4-méthoxyphényl)-2-oxoéthyle
anisatilo	2-(4-metoxifenil)-2-oxoetilo



AMENDMENTS TO PREVIOUS LISTS

Proposed International Nonproprietary Names (Prop. INN): List 63

(WHO Drug Information, Vol. 4, No. 2, 1990)

- | | | |
|-------|-------------------------|--|
| p. 18 | saruplasum
saruplase | <i>replace the definition by the following:</i>
prourokinase (enzyme-activating) (human clone pUK4/pUK18), non-glycosylated |
|-------|-------------------------|--|

Proposed International Nonproprietary Names (Prop. INN): List 68

(WHO Drug Information, Vol. 6, No. 4, 1992)

- | | | |
|------|-----------------------------|--|
| p. 9 | nasaruplasum
nasaruplase | <i>replace the definition by the following:</i>
prourokinase (enzyme-activating) (human clone pA3/pD2/pF1 protein moiety), glycosylated |
|------|-----------------------------|--|

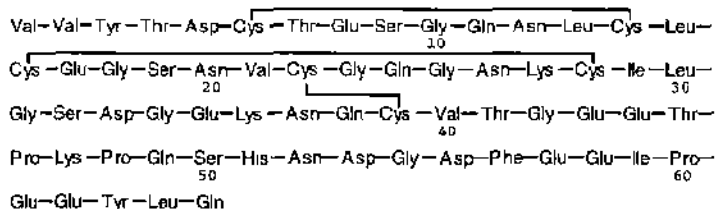
Proposed International Nonproprietary Names (Prop. INN): List 71

Dénominations communes internationales proposées (DCI Prop.): Liste 71

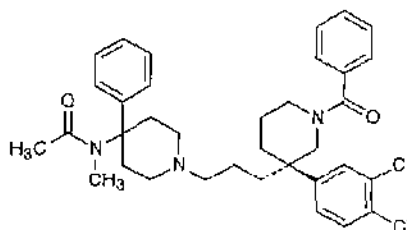
Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Lista 71

(WHO Drug Information, Vol. 8, No. 2, 1994)

- | | | |
|-------|--|---|
| p. 26 | desirudinum
desuridin
désirudine
desirudina | <i>add the following graphic formula:</i>
<i>insérer la formule développée suivante:</i>
<i>insertar la siguiente fórmula desarrollada:</i> |
|-------|--|---|



- | | | |
|-------|--|---|
| p. 16 | lutropinum alfa
lutropin alfa
lutropine alfa
lutropina alfa | <i>add the following CAS registry number to the β-subunit:</i>
<i>insérer le numéro dans le registre du CAS pour la sous-unité β:</i>
<i>insertar el siguiente número de registro del CAS para la subunidad β:</i>
β: 53664-53-2 |
|-------|--|---|

**Proposed International Nonproprietary Names (Prop. INN): List 75****Dénominations communes internationales proposées (DCI Prop.): Liste 75****Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Lista 75***(WHO Drug Information, Vol. 10, No. 2, 1996)***p. 7 choriogonadotropinum alfa**

choriogonadotropin alfa

*replace the definition by the following:*human chorionic gonadotropin (protein moiety reduced), glycoform α α -subunit:chorionic gonadotropin (human α -subunit protein moiety reduced) β -subunit:chorionic gonadotropin (human β -subunit protein moiety reduced)

choriogonadotropine alfa

*remplacer la description par:*gonadotropine chorionique humaine (partie protéique réduite), forme glycosylée α sous-unité α :gonadotropine chorionique (partie protéique réduite de la sous-unité α humaine)sous-unité β :gonadotropine chorionique (partie protéique réduite de la sous-unité β humaine)

coriogonadotropina alfa

*sustituyase la descripción por la siguiente:*gonadotropina coriónica humana (fracción proteica reducida), glucoforma α subunidad α :gonadotropina coriónica (fracción proteica reducida de la subunidad α humana)subunidad β :gonadotropina coriónica (fracción proteica reducida de la subunidad β humana)

p. 9	ecamsulum ecamsule écamsule ecamsul	<i>add the following CAS registry number: insérer le numéro dans le registre du CAS suivant: insértese el número del registro del CAS siguiente: 92761-26-7</i>
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MODIFICATIONS APPORTÉES AUX LISTES ANTÉRIEURES

Dénominations communes internationales proposées (DCI Prop.): Liste 58
(*Informations pharmaceutiques OMS, Vol. 1, No.3, 1987*)

p. 14	saruplasum saruplase	<i>remplacer la description par: pro-urokinase (activateur d'enzyme) (fraction protéique issue du clone humain pUK4/pUK18), non-glycosylée</i>
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Dénominations communes internationales proposées (DCI Prop.): Liste 68
(*Informations pharmaceutiques OMS, Vol. 6, No.4, 1992*)

p. 9	nasaruplasum nasaruplase	<i>remplacer la description par: pro-urokinase (activateur d'enzyme) (fraction protéique issue du clone humain pA3/pD2/pF1), glycosylée</i>
------	-----------------------------	---

Pour toutes modifications apportées aux **Dénominations communes internationales proposées (DCI Prop.): Listes 71-75** voir page 221, section *AMENDMENTS TO PREVIOUS LISTS*

MODIFICACIONES A LAS LISTAS ANTERIORES

Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Liste 63
(*Información Farmacéutica, OMS, Vol. 4, No. 2, 1990*)

p. 18	saruplasum saruplase	<i>sustituyase la descripción por la siguiente: prouroquinasa (activador de enzima) (fracción proteica procedente del clon humano pUK4/pUK18), no glucosilada</i>
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Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Liste 68*(Información Farmacéutica, OMS, Vol. 6, No. 4, 1992)*

p. 18	nasaruplasum	<i>sustituyase la descripción por la siguiente:</i>
	nasaruplasa	prouroquinasa (activador de enzima) (fracción proteica procedente del clon humano pA3/pD2/pF1), glucosilada

Para cualquier modificación de las **Denominaciones Comunes Internacionales Propuestas (DCI Prop.):**

Listas 71-75 vease página 221, sección **AMENDMENTS TO PREVIOUS LISTS.**

Procedure and Guiding Principles / Procédure et Directives / Procedimientos y principios generales

The text of the *Procedures for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances* and *General Principles for Guidance in Devising International Nonproprietary Names for Pharmaceutical Substances* will be reproduced in uneven numbers of proposed INN lists only.

Les textes de la *Procédure à suivre en vue de choix de dénominations communes internationales recommandées pour les substances pharmaceutiques* et des *Directives générales pour la formation de dénominations communes internationales applicables aux substances pharmaceutiques* ont été publiés avec la liste 75 des DCI proposées et seront, à nouveau, publiés avec la prochaine liste.

El texto de los *Procedimientos de selección de denominaciones comunes internacionales recomendadas para las sustancias farmacéuticas* y de los *Principios generales de orientación para formar denominaciones comunes internacionales para sustancias farmacéuticas* aparece solamente en los números impares de las listas de DCI propuestas.

