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# Recommendations for national registers of medicinal products with validated ATC codes and DDD values

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## Abstract

Medicines have important effect on population health and it is important to have a system for assessing their effects and monitoring their use, expenditure and price.
The basis for all these objectives is the availability of an internationally valid classification system of medicines and a measurement system of their utilisation.
Since 1996 the WHO Headquarter has adopted and proposed the ATC (Anatomical Therapeutical Chemical) classiifcation and the DDD (Defined Daily Dose) as the global standard for medicine classification and utilisation sudies, respectively.
The EURO-MED-STAT project has defined the criteria for the production, validation and maintenance of national registers with validated ATC codes and DDD values, as suggested by WHO.
A register with a valid ATC code and DDD value is able to provide reliable information allowing calculation of utilisation and expenditure indicators (Utilisation in DDD; DDD/1000inh/day and Expenditure per DDD).

*Key words: pharmaceuticals, ATC, DDD, drug utilisation, drug expenditure, Europe, pricing*

### Introduction

More than 100,000 pharmaceutical packages are licensed in the European Union countries and tons of medicines are daily used with a yearly expenditure of more than 100 billion euro.

This vast amount of medicines is a challenge to public health for several reasons:

- medicines can positively influence public health by their intended therapeutic effect
- medicines can adversely affect public health because of medicine related problems; medicine related problems are an important cause of mortality and most of them can be prevented [1-4]
- there is an important economic burden of medicines on healthcare systems [5]
- medicines are able, via the wastewater, to pollute the environment, including drinking water. Several medicines have endocrine-disrupters or carcinogenic properties [6-7]
- there are wide discrepancies between European countries in licensed medicines, their price, utilisation and expenditure [8].

Because of these challenges of medicines on public health there is a need

- to increase awareness and spread knowledge on the impact of medicine utilisation on public health
- to promote European harmonised data collection about licensed medicines, their prices, utilisation and expenditure
- to develop indicators for monitoring price, utilisation and expenditure of medicines at a European level
- to promote benchmarking exercise on utilisation of medicines at national and regional level
- to assess the outcome of medicine utilisation, linking pharmacoepidemiological data to morbidity-mortality data
- to develop a public health-oriented European database of the licensed medicines with relevant information about their best use.

For all these purposes it is essential to have an internationally valid classification system of medicines and a measurement system of their utilisation.

Since 1981, the WHO Regional Office for Europe has recommended the ATC (Anatomical Therapeutic Chemical) classification system and the DDD (Defined Daily Dose) as the standard for medicine classification and drug utilisation

studies, respectively. [9] Since 1996, the ATC/DDD methodology has been adopted and proposed by the WHO Headquarters for global use.

The EURO-MED-STAT project has inventoried more than 72 different registers of medicinal products in the European Union Member States (EU-15) and Norway. These registers strongly differ in both their content and structure. (Table 1).

**Table 1. LIST of the INVENTORIED REGISTERS by COUNTRY**

| | | PRICE | EXPENDITURE | UTILISATION | | All Medicines | Prescription Only | OTC | | All Medicines | Reimbursed only | Not reimbursed | | Out of Hospital | Hospital | Both (pooled) | | DDD or DDD/1000inh/day | Number of packs | Number of pts treated |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Austria | 1. Pharmazeutisches Informationssystem (Pharmaceutical Information System) | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Austria | 2. Austria Codex by the Austrian Chamber of Pharmacists | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Austria | 3. Heilmittelverzeichnis (List of Pharmaceuticals) by the Federation of the Austrian Social Insurance Institutions | ✔ | | | | ✔ | | | | | ✔ | | | | | | | | | |
| Austria | 4. Pegasus by the Federation of the Austrian Social Insurance Institutions | | | | | | | | | | | | | | | | | | | |
| Austria | 5. Foko by the Federation of the Austrian Social Insurance Institutions | | | | | | | | | | | | | | | | | | | |
| Austria | 6. Warenverzeichnis (List of commodities/products) | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Austria | 7. IMS data | | | ✔ | | ✔ | | | | ✔ | | | | | | ✔ | | | ✔ | ✔ |
| Austria | 8. Krankenansstalten-Kostenstellenstatistik (Statistic Cost Account in Hospital) | | ✔ | | | ✔ | | | | ✔ | | | | | ✔ | | | | | |
| Austria | 9. Mikrozensus-Erhebung (Survey Questions concerning Health) by Statistik Austria | | | ✔ | | ✔ | | | | ✔ | | | | ✔ | | | | | | |
| Austria | 10. Pharma Preisinformation-PPI (Pharma Price Information) by ÖBIG | ✔ | | | | ✔ | ✔ | | | ✔ | ✔ | | | | | | | | | |
| Belgium | 1. BCFI-Databank / Banque des Données CBIP | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Belgium | 2. Farmanet / Pharmanet | ✔ | ✔ | ✔ | | | ✔ | | | | ✔ | | | ✔ | | | | ✔ | ✔ | ✔ |
| Belgium | 3. IFEB / IPHEB | ✔ | ✔ | ✔ | | | ✔ | | | | ✔ | | | ✔ | | | | ✔ | ✔ | |
| Denmark | 1. Lægemiddelstyrelsen Lægemiddelstatistikregister (The Register of Medicinal Products Statistics) | ✔ | ✔ | ✔ | | ✔ | | | | ✔ | | | | ✔ | ✔ | | | ✔ | ✔ | ✔ |
| Denmark | 2. Specialitetstaksten (Pricelist) | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Finland | 1. Lääkemyyntirekisteri (Drug Sales Register) by the National Agency for Medicines | | ✔ | ✔ | | ✔ | | | | | | | | ✔ | ✔ | ✔ | | ✔ | | |
| Finland | 2. Lääkevalmisteiden perusrekisteri (List of Registered Medicines) by the National Agency for Medicines | | | | | ✔ | | | | | | | | | | | | | | |
| Finland | 3. Paradox 7, HILA 2000 (Register of fixed wholesale price) | ✔ | | | | ✔ | | | | | ✔ | | | ✔ | | | | | | |
| Finland | 4. Reseptirekisteri (Prescription Register) | ✔ | ✔ | ✔ | | | | | | | ✔ | | | ✔ | | | | | | |
| Finland | 5. Suomen Apteekkariliiton Lääkevalmisteiden tiedosto (Register of Pharmaceutical Products on sale in Finland) by the Finnish Association of Pharmacists | ✔ | | | | ✔ | | | | ✔ | | | | ✔ | | | | | | |
| France | 1. Database at the AFSSAPS-(French Agency of Sanitary Security of Health Products) | | ✔ | | | ✔ | | | | ✔ | | | | | | ✔ | | | | |
| France | 2. Database of reimbursed medicines - CNAMTS | | ✔ | ✔ | | | ✔ | | | | ✔ | | | ✔ | | | | | ✔ | |

| | | PRICE | EXPENDITURE | UTILISATION | | All Medicines | Prescription Only | OTC | | All Medicines | Reimbursed only | Not reimbursed | | Out of Hospital | Hospital | Both (pooled) | | DDD or DDD/1000inh/day | Number of packs | Number of pts treated |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| France | 3. Guide des Equivalents Therapeutiques | | | ✔ | | ✔ | | | | ✔ | | | | | | | | | | |
| France | 4. GERS (Groupement pour l'Elaboration et la Realisation de Statistiques | ✔ | ✔ | | | ✔ | | | | ✔ | | | | | | ✔ | | | ✔ | |
| France | 5. Dictionnaire Vidal | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Germany | 1. GKV – Arzneimittelindex (Drug Index of the Statutory Health Insurance) | ✔ | ✔ | ✔ | | ✔ | | | | ✔ | | | | ✔ | | | | ✔ | ✔ | |
| Greece | Gredis II | | | | | | | | | | | | | | | | | | | |
| Ireland | | | | | | | | | | | | | | | | | | | | |
| Italy | 1. Informatore Farmaceutico (List of medicinal product licensed in Italy) by OEMF | ✔ | | | | ✔ | | | | ✔ | | | | | | | | | | |
| Italy | 2. Osservatorio sull'Utilizzo dei Farmaci (Utilisation and Expenditure database) at the Ministry of Health | | ✔ | ✔ | | ✔ | | | | ✔ | | | | ✔ | | | | ✔ | | |
| Italy | 3. Database interno sui prezzi (Price Directories) at the Ministry of Economics | ✔ | | | | | ✔ | | | | ✔ | | | | | | | | | |
| Italy | 4. Database Agenzia per i Servizi Sanitari Nazionali (Monthly survey of reimbursed medicines) | | ✔ | ✔ | | | ✔ | | | | ✔ | | | ✔ | | | | | ✔ | |
| NDL | 1. AGB-z (Algemeen Gegevens Beheer Zorgverleners (General Data Controle-medical persons) | ✔ | ✔ | | | | | | | | | | | | | | | | | |
| NDL | 2. BIOS at The Medicines Evaluation Board | | | | | ✔ | | | | | | | | | | | | | | |
| NDL | 3. Vektis BV (Pharmacy Information System) | ✔ | ✔ | ✔ | | | ✔ | | | | ✔ | ✔ | | ✔ | | | | ✔ | ✔ | |
| NDL | 4. GIP- Dutch Drug Information Project by Healthcare Insurance Council | | ✔ | ✔ | | | ✔ | | | | ✔ | | | ✔ | | | | ✔ | ✔ | ✔ |
| NDL | 5. Vektis BV (Information System Pharmaceutical Product) | ✔ | ✔ | ✔ | | ✔ | | | | ✔ | | | | | | | | | | |
| NDL | 6. IMS Health | ✔ | ✔ | ✔ | | ✔ | | | | ✔ | | | | ✔ | ✔ | | | ✔ | ✔ | ✔ |
| NDL | 7. LINH Landelijk Informatie Netwerk Huisartssenzorg (National information Network in General Practice | | | ✔ | | | ✔ | | | | ✔ | | | ✔ | | | | ✔ | | ✔ |
| NDL | 8. PHARMO Database | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ |
| NDL | 9. SFK Stichting Farmaceutische Kengetallen Database (Foundation for Pharmaceutical Statistics) | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ | | ✔ | ✔ | | | ✔ | ✔ | ✔ |
| Norway | 1. Division for Epidemiology; Norwegian Institute of Public Health | | ✔ | ✔ | | ✔ | ✔ | ✔ | | | | | | | | ✔ | | ✔ | | |
| Portugal | 1. National Drug Expenditure Database by Observatorio do Medicamento-INFARMED | ✔ | ✔ | | | | ✔ | | | | ✔ | | | ✔ | ✔ | | | | ✔ | |
| Portugal | 2. IMS Health database | ✔ | ✔ | ✔ | | ✔ | | | | ✔ | | | | ✔ | ✔ | | | | ✔ | |
| Spain | 1. Base de Datos ECOM | ✔ | ✔ | ✔ | | | ✔ | | | | ✔ | | | | ✔ | | | | ✔ | |
| Spain | 2. V-I; Vademecum International Especialidades Farmacéuticas y Biológicas | | | ✔ | | ✔ | | | | ✔ | | | | | | | | | | |
| Spain | 3. Base de Datos del Medicamento del Consejo | | | | | | | | | | | | | | | | | | | |
| | General de Colegios Oficiales de Farmacéuticos | | | ✔ | | ✔ | | | | ✔ | | | | | | ✔ | | | | |
| Spain | 4. IMS | ✔ | ✔ | ✔ | | | | | | | | | | | | | | | | |
| Sweden | 1. Inleveransstatistik (Wholesale statistics) | | ✔ | ✔ | | ✔ | | | | ✔ | | | | | | ✔ | | ✔ | ✔ | |
| Sweden | 2. Öppenvård – förskrivning (Prescription sales) | | ✔ | ✔ | | ✔ | | | | ✔ | | | | ✔ | | | | ✔ | ✔ | |
| Sweden | 3. Slutenvårdsförsäljning (Hospital sales) | | ✔ | ✔ | | ✔ | | | | ✔ | | | | | ✔ | | | ✔ | ✔ | |
| Sweden | 4. Egenvårdsförsäljning (OTC sales) | | ✔ | ✔ | | | | ✔ | | ✔ | | | | ✔ | | | | ✔ | ✔ | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sweden | 5. Diagnos Receptundersökningen-DRU (Diagnosis and prescription survey) | | | ✔ | ✔ | | | ✔ | | | ✔ | | | ✔ | ✔ | ✔ |
| Sweden | 6. Jämtlandsstudien (The Jamtland study) | | ✔ | ✔ | ✔ | | | ✔ | | | ✔ | | | ✔ | ✔ | ✔ |
| Sweden | 7. Tierpsprojekt (Tierp project) | | | ✔ | ✔ | | | ✔ | | | ✔ | | | ✔ | ✔ | ✔ |
| UK | 1. Prescriptions dispensed in the community at DoH | | ✔ | ✔ | ✔ | | | | ✔ | | ✔ | | | | ✔ | |
| UK | 2. British National Formulary | ✔ | | | | ✔ | ✔ | | | | | | | | | |
| UK | 3. Hospital database at DoH | | ✔ | ✔ | ✔ | | | ✔ | | | | ✔ | | | | |
| UK | 4. England-Prescription Pricing Authority Database | | ✔ | ✔ | ✔ | | | | ✔ | | ✔ | | | | ✔ | |
| UK | 5. Chemist and Druggist by National Pharmaceutical Association | ✔ | | | ✔ | | | ✔ | | | | | | | | |
| UK | 6. Mediplus by IMS | | | ✔ | ✔ | | | | | | ✔ | | | | ✔ | ✔ |
| UK | 7. General Practice Research Database at Medicines Control Agency | | ✔ | | ✔ | | | ✔ | | | ✔ | | | | ✔ | ✔ |
| UK | 8. Doctors Independent Network | | | ✔ | ✔ | | | | | | ✔ | | | | ✔ | ✔ |
| UK | 9. IMS | | ✔ | ✔ | ✔ | | | ✔ | | | ✔ | ✔ | | | ✔ | |
| UK | 10. ABPI Datasheet Compendium | | | | | ✔ | | | | | | | | | | |
| UK | 11. File at the Medicines Control Agency | ✔ | | | ✔ | | | ✔ | | | | | | | | |
| UK | 12. Prescription Only Medicines (human use) order 1997 | | | | | ✔ | | | | | | | | | | |
| Australia | 1. Database of the Drug Utilisation Sub Committee (DUSC) at the Department of Health and Ageing | | | ✔ | | ✔ | | | ✔ | | ✔ | | | ✔ | | |

For monitoring and comparing the medicines available in the European Union, their prices, utilisation, expenditure and licensed clinical properties, it is necessary that national data can be compared by national registers with similar structure and content.

For this purpose the ATC/DDD system needs to be implemented in a valid and transparent way in all of the countries and that national registers for medicinal products are able to link each pharmaceutical pack to its ATC code and DDD value.

## Aim of the Recommendations for national registers of medicinal products with validated ATC codes and DDD values

The aim of these Recommendations is to define the criteria for the production, validation, and maintenance of national registers of medicinal products with validated ATC codes and DDD values in the Member States of the European Union. This will allow validated comparisons at a European level of licensed medicines, their price, expenditure, utilisation and licensed clinical properties in a public health perspective.

### Content of the National Registers

The register of licensed medicines should contain information on all medicine packages licensed and available on the national market for human use. It should be updated on a regular basis (e.g. monthly or every second week), and the date of the latest update should always be included in the register.

In cases where the register contains packages, licensed but not available on the market, a mechanism to identify these records should be in place. Utilisation data will normally only cover packages available on the market, and this may be one way of separating licensed medicine packages from licensed and marketed medicine packages. If the date of marketing is included in the register (as recommended), this data element will be the best way of separating these records.

Registers of Medicinal Products produced by Medicine Agencies will normally include all licensed medicines.

Historical versions of the register with packages no longer licensed or available should be kept. This is of importance for the updating of ATC codes and DDD values of historical utilisation and expenditure data.

When producing and presenting trends for utilisation and expenditure data over years, it is important that the data are presented using the same ATC/DDD version.

### Structure of the National Registers

The structure of the National Register should be in compliance with the following standards.

***European PreStandard ENV 12610 for the Identification of medicinal products [10]***

European PreStandard ENV 12610 (Medical Informatics – Medicinal product identification by the European Committee for Standardization; Brussels 1997) aims to define the language to be used to structure coding systems for the identification of medicinal products. The PreStandard contains the definition of the concepts, the description of the characteristics and the relationship needed to identify each of these unambiguously, particularly for the purpose of in-formation exchange between information systems.

***European Pharmacopoeia of the Council of Europe for the pharmaceutical forms [11]***

The pharmaceutical form is the combination of both the form in which a medicinal product is presented by the manufacturer (form of presentation) and the form in which it is administered, including the physical form (form of administration).

The List of pharmaceutical forms by the European Pharmacopoeia of the Council of Europe- European Directorate for the Quality of Medicines (List of Standard Term, Introduction and Guidance for use - 2002 Edition) presents the basic terms needed to characterise the pharmaceutical form of a medicinal product contains the translation in 21 different languages.

It is based on the following principles:

- consistency of terminology thorough out the list
- each term should be as short as possible, commensurate with the necessary information
- each term needs to convey several "elements" of information. The number of elements will vary from one product type to another.

A complete list of the official English terms for pharmaceutical forms is given in Annexe 7 – Council of Europe. Standard terms. List of pharmaceutical forms (page 77).

***Council Directive 92/26/EEC and Council of Europe for the Legal categories of medicines [12]***

EEC Directive 92/26 [Council Directive 92/26/EEC concerning the classification for the supply of medicinal products for human use: OJ L 113, 30.4.1992; Bull. 3-1992, point 1.2.19].

Council of Europe-Committee of Ministers. Resolution (AP 2000)1 on the classification of medicines, which are obtainable only on medical prescription. Adopted by the Committee of Ministers on 15 March 2000 at the 702nd Meeting of the Ministers' Deputies.

***WHO International Non-proprietary names for the Name of the active ingredients***

International Non-proprietary Names (INN) for active ingredients assigned by WHO.

*http://www.who.int/medicines/services/inn/en*

***ATC Index and Guidelines for ATC Classification and DDD assignment for ATC codes and DDD values [13]***

ATC index and Guidelines for ATC classification and DDD assignment are released annually by the WHO Collaborating Centre for Drug Statistics Methodology in Oslo.

### EURO-MED-STAT - Minimal Data Set for National Register of Medicinal Products with Validated ATC Codes and DDD Values

The Register should contain at least the following elements (in separate fields):

**1 Registration number or other unique identifier**
**2 ATC code**
**3 Active ingredient(s)**
**4 Medicinal Product Name with its specifiers**
**5 Trade Name**
**6 Pharmaceutical Form**
**7 Strength**
**8 Pack size**
**9 Legal category**
**10 Reimbursement**
**11 Pharmacy retail price**
**12 Date of approval**
**13 Date of first marketing**
**14 Date of removal from the market**
**15 Holder of marketing authorisation**
**16 Generic**
**17 Parallel import**
**18 Value of the DDD**
**19 Route of administration**
**20 Number of DDDs in the pack**

### ATC and DDD linkage process

The purpose of this process is to link the correct and valid ATC 5th level code to each medicinal product package.

This will allow the correct Defined Daily Dose (sometimes in function of the route of administration or the chemical salt) to be linked

and finally, to calculate the number of DDDs per package (adequate information about the product is necessary in order to calculate this number properly).

It is recommended that strict control routines for adding and changing the ATC/DDD information in the National Registers of Medicines should be in place, as this is the basis for calculating utilisation data in a correct and comparable way.

The team responsible for the National Registers of Medicines should be properly trained in the ATC/DDD methodology and collaborate closely with the WHO Collaborating Centre for Drug Statistics Methodology in Oslo.

When a new substance is introduced on the market for which no official ATC code or DDD yet has been assigned (the latest assignments are available on the website of the Centre), a request for a new ATC/DDD should immediately be sent to the WHO Collaborating Centre. Application forms for new ATC codes and DDDs are available on the Centre's website (www.whocc.no) and a preliminary ATC code is usually assigned within 4-6 weeks.

New DDDs are assigned twice annually.

Each year in early December, the annual update of the next version of the ATC INDEX is made available by the WHO-Collaborating Centre. Updates of the ATC codes and DDD values in the National Registers of Medicines should be made early in the following year.

### Production of utilisation and expenditure data

Sales figures (from companies, wholesalers, pharmacies or other sources) for the number of packages of medicinal products can be easily linked to each record of the national registers. The following recommended utilisation and expenditure indicators can be produced:

1- The indicator **Utilisation in DDDs** can be calculated by multiplying the number of packages sold with the number of DDDs in the package.

$$\textit{Number of packages sold} \times \textit{Number of DDD in the pack}$$

2- The indicator **DDDs/1000 inhabitants/day**, can be calculated as follows:

$$\frac{\textit{Total consumption measured in DDDs}}{\textit{Number of days in the period of data collection} \times \textit{number of inhabitants}} \times 1000$$

The number of inhabitants in the denominator should refer to the total population covered by the in the area where the total consumption data is collected. If the coverage of the consumption is not 100%, then the population size should be corrected accordingly and described.

3- The indicator **cost expenditure per DDD** can be calculated as follows:

$$\frac{\textit{Number of packages sold} \times \textit{Pharmacy Retail Price}}{\textit{Consumption in DDDs}}$$

*A full description of these indicators is given in the related document: The Library of European Union Pharmaceutical Indicators. Expenditure and Utilisation Indicators at http://www.euromedstat.cnr.it/indicators/indicators.asp*

### References

1) Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients.
2) BMJ. 2004 Jul 3;329(7456):15-9.
3) Brennan TA, Leape LL, Laird NM, Hebert L, Localio R, Lawthers AG, Newhouse JP, Weiler PC, Hiatt HH. Incidence of adverse events and negligence in hospitalized patients. Results of The Harvard Medical Practice Study I. New Engl J Med 1991; 324:370-6.
4) Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes Ba et al. The nature of adverse events in hospitalized patients. Results of The Harvard Medical Practice Study II. New Engl J Med 1991; 324:377-84.
5) LT, Corrigan JM, Donldson MS (editors). To err is human: building a safer health system. Washington D.C. National Academy Press 2000.
6) Thorpe K.E. Cost sharing, caps on benefits, and the chronically ill - A policy mismatch. N Engl J Med 2006; 354:2385-6.
7) Health Council of The Netherlands. Environmental risk of medicines. The Hague. 2001.
8) Zuccato E, Calamari D, Natangelo M, Fanelli R Presence of therapeutic drugs in the environment Lancet 2000; 355:1789-90.
8) Folino-Gallo P, Walley T, Frolich JC, Carvajal A, Edwards IR. Availability of medicines in the European Union: results from the EURO-Medicines project. Eur J Clin Pharmacol. 2001;57:441-6.
9) WHO Collaborating Centre for Drug Statistics Methodology. ATC Index with DDD. Oslo 2006.
10) European PreStandard ENV 12610 (Medical Informatics – Medicinal product identification by the European Committee for Standardization; Brussels 1997)
11) European Directorate for the Quality of Medicines. European Pharmacopoeia of the Council of Europe- List of Standard Term, Introduction and Guidance for use - 2002 Edition.
12) Council Directive 92/26/EEC concerning the classification for the supply of medicinal products for human use: OJ L 113, 30.4.1992; Bull. 3-1992.
13) WHO Collaborating Centre for Drug Statistics Methodology. ATC Guidelines for ATC classification and DDD assignment. Oslo. Several editions from 1998 to 2006.