

EphMRA/PBIRG
CLASSIFICATION COMMITTEE

WHO WE ARE
WHAT WE DO

2009

Table of Contents

Background.....	2
Anatomical Classification System Overview	2
Voting Requirements.....	3
Committee Membership	3
Rules of Classification.....	5
A Structure of the Anatomical Classification System	5
B Main Principles of Classification.....	5
C Classification of Products – Plain versus Combination	6
C1 Classification of plain products	6
C2 Classification of combination products.....	6
D Classification of new products.....	7
D1 General.....	7
<i>Conditions</i>	7
<i>Reasons to Create a new Class</i>	7
<i>Use and Reuse of Classification Codes</i>	7
D2 Procedure.....	7
D3 Implementation.....	8
D4 Voter eligibility.....	8
E Changes of classification of existing products.....	8
Access to the EphMRA/PBIRG Guidelines	9
Harmonization with WHO.....	9
Comparison of EphMRA/PBIRG Anatomical Classification with WHO ATC	10

Classification Committee

Background

Pharmaceutical products are grouped into categories in the sales, medical, and promotional audits according to the EphMRA/PBIRG Anatomical Classification System. Virtually all pharmaceutical audits around the world are based on this system. IMS has adopted this system. Local suppliers have also adopted it.

The Anatomical Classification brings order and standardization to the pharmaceutical market. This classification enables the market researcher to analyze therapeutic markets and to compare similar products. Responsibility for maintaining the integrity of the system, for modifying it to meet the demands of the evolving pharmaceutical market, and for reviewing and approving the classification of individual products lies with the Classification Committee. The World Health Organization (WHO) adapted the system to its own needs (see section on **Harmonization with WHO**).

Pharmaceutical sales audits were introduced in the 1950s. Most audits were based on similar classification systems, although they varied. Development of the Anatomical Classification began in 1968 and was formally introduced in 1974. It was developed by market researchers of many Europe-based international pharmaceutical companies. Market researchers from the international pharmaceutical companies in Europe and USA participated in translating the old system into the Anatomical System. Today, the only countries not on the Anatomical Classification are USA and Canada. However, USA and Canada data are available in the Anatomical Classification via the IMS electronic database, MIDAS.

Anatomical Classification System Overview

The Anatomical Classification System is based on a cascade: the 2nd level gives details of the 1st, the 3rd of the 2nd, and the 4th of the 3rd. Products are grouped by anatomical site of action, indication, or composition.

An important point to note about the system is that products are classified, not molecules. "Product" is defined as a pack or unit that can be dispensed, prescribed, etc. The products are classified according to their main therapeutic indication. Each product is assigned to one category. There is no apportionment of sales by usage, such as Diagnosis Value.

In order to create a new category within the system, there must be a compelling need for a new category and a product with an approved indication launched in one country and a second or similar substance in pre-registration and therefore expected to be launched soon after. A one-product class will not be created. Classes can be approved in anticipation of the criteria being fulfilled at the time of implementation of the new class. New classes can be suggested by EphMRA/PBIRG members, non-EphMRA/PBIRG members, or the Committee. The proposals should be clearly stated and the impact of the change to the system should be outlined. This includes suggested classification of the products affected by a proposed change. The proposal is carefully reviewed by the entire Committee, which consults, as needed, with appropriate involved member companies and sometimes with medical opinion leaders. The Committee reviews the proposed changes with these outside consultants and may solicit alternative suggestions. The purpose is to find out if there is general consensus that the system should be modified and what the changes should be. The responsible Committee member finalizes the proposal. The finalized proposal with background information is sent out to the full EphMRA/PBIRG membership for voting in the second quarter of the year.

(See section **Rules of Classification** further in this brochure for more detailed information.)

Voting Requirements

Only full members may vote

Each member company is entitled to one vote. Only one vote will be counted for each company. The company can choose to vote with either EphMRA or PBIRG.

A “company” is defined as a corporate entity. In other words, there is one vote per corporation, regardless of the number of affiliates or subsidiaries (unless any are separate corporate entities).

The proposals need the approval of a 2/3 majority of the voting companies to pass

If a 2/3 majority is not reached, a second count is made of interested companies

If 2/3 of the actively involved companies approve, the class is approved

If the proposal is accepted, a Committee member is assigned to reclassify each pack of each product. The change is implemented in the first audit of the New Year.

Committee Membership

The Anatomical Classification Committee consists of approximately ten members as this has been found to be a size that is manageable and that supports open discussion. The committee consists primarily of market researchers in EphMRA-member companies in Europe plus one member from PBIRG. The PBIRG representative is the Chair of the PBIRG Classification Committee. IMS is also represented on the Committee as a non-voting member. A member from Asia/Japan would also be welcome. The primary qualifications for membership are knowledge of the international pharmaceutical market and experience with the databases. Each member has the primary responsibility for one or more therapeutic categories. The most important goal is to have a specialist for each therapeutic area. Another goal is to have different countries represented on the Committee. For the benefit of the individual Committee members as well as the Committee, nominees for Committee membership are normally expected to try out with the Committee for a few meetings before officially joining the Committee. Generally, when positions on the Committee are available, nominations for members who meet the qualifications are sought from member companies. Volunteers for the Committee could also be considered. In order to add value to the industry and the Committee, members are expected to serve on the Committee for at least two years. This medium to long-term commitment will also enhance the experience for the Committee member.

Members are notified of the classes of product launches in their assigned categories, and these must be reviewed for correctness. Each member also has the primary responsibility for any restructuring of the assigned categories. All requests for change of individual products are reviewed by the entire Committee in order to approve the change.

The Committee meets four times each year for approximately two days. Since a different member of the Committee hosts each meeting, the location of the meeting rotates around member countries. It is the responsibility of the hosting Committee member to organize a venue and the logistics, and to provide a meeting room. EphMRA does not fund Committee members. Representatives of pharmaceutical companies and data suppliers may, after invitation, come to present their issues at the Committee’s working sessions.

In order for the Committee to function at a high level, the members must be able to work closely together in an atmosphere of free and open exchange. This is achieved by members’ observing the following code of behavior:

- While it is expected that members will consult with experts within their companies for advice, Committee members do not represent their companies, per se. Committee members consider the needs of the Classification System and industry analysts as the priority.

- In order not to convey erroneous impressions about Committee viewpoints, preliminary decisions are not divulged outside of the Committee until the Committee has come to an agreement.
- In order to encourage open debate and exploration of ideas, Committee members must be free to express their opinions within the Committee without concern of subsequent pressure. A value of the dialectic is that members can change their viewpoints during the discussions. Therefore, opinions of individual Committee members remain within the Committee.

The Committee has established an Associate position open to analysts with 2-3 years of relevant experience. The Associate's role entails the following:

- conduct secondary research into product classification and potential new categories,
- share responsibility for therapeutic classes, under the mentorship of a full Committee member, and
- attend meetings and join in Committee discussions of therapeutic classes and individual product classifications.

Participation in these open discussions with experienced Committee members will provide the Associate with in-depth understanding of the global pharmaceutical industry, a broad range of therapeutic areas, research trends and the industry-WHO relationship. The Associate would also gain knowledge of the audit databases.

- The Committee would benefit by having more input and by having a person who could eventually become a full committee member.
- The Associate's Company would benefit from the extensive training and the wealth of knowledge that the analyst would bring back to the Company.
- There will be a Certificate of Recognition from the Executive in appreciation of the Associate's contributions.
- The cost of attending Committee meetings will be borne by the Associate's company.

Contact the Classification Committee if you would like to be nominated for this position.

Please contact your local country member, if available, or the Chairperson of the Committee for any requests for change of classification. See EphMRA (www.ephmra.org) and PBIRG (www.pbirg.com) websites for a directory of Committee members and their responsibilities.

Rules of Classification

A Structure of the Anatomical Classification System

In the Anatomical Classification System, products are divided into different groups according to anatomical site of action, their indications, therapeutic use, composition, mode of action, etc. Products are classified in groups at 4 different levels. There are main groups (1st level), and then 2nd, 3rd, and 4th levels. The 2nd, 3rd, and 4th levels are used to identify pharmacological subgroups if that is considered more appropriate than a therapeutic subgroup.

The following scheme illustrates the complete classification of a product:

C Cardiovascular System
(1st level, anatomical main group)

C10 LIPID-REGULATING/ANTI-ATHEROMA PREPARATIONS
(2nd level, therapeutic main group)

C10A CHOLESTEROL AND TRIGLYCERIDE REDUCTION PREPARATIONS
(3rd level, pharmacological/therapeutic subgroup)

C10A1 Statins (HMG-CoA reductase inhibitors)
(4th level, chemical/pharmacological/therapeutic subgroup)

For the purpose of the Anatomical Classification, a product represents a discrete pharmacological pack or unit that can be dispensed, prescribed, purchased, etc. So, the 10mg 90-tablet pack of LIPITOR is per definition a product. The 2nd level is used to regroup several classes together, in order to classify according to:

- a) indication (e.g., B1 antithrombotics)
- b) therapeutic substance group (e.g., J1 antibiotics)
- c) anatomical system (e.g., S1 ophthalmologicals)

The **2nd level** should enable the creation of the cascade classification. Therefore, before creating a new second level, all existing possibilities of classification should be analyzed. There could be cases where it is necessary to create a 2nd level without a cascade to 3rd or 4th level. However, these cases should be kept to the minimal extent possible.

The **3rd level** describes a specific group of products within the 2nd level. This specification can be a chemical structure (J1D cephalosporins) or it can describe an indication (N2C antimigraine) or a method of action (A3F gastroprokinetics).

The **4th level** gives more details of the 3rd level (formulation, chemical description, mode of action, etc.)

B Main Principles of Classification

The basic principle is that there is only one Anatomical Classification code allocated to a product/pack.

The guiding principle is to achieve consistent classification for products so that a product is classified in the same category in all countries. However, there are occasions where it would not be appropriate to follow this principle. For example, a product in one country can consist of the same substance and have the same brand

name as a product in another country but with different indications or substantially different use. Therefore, the class assigned to one of these products could be different from that assigned to the product with the same name in another country.

If one looks at substances, the same substance can be in several products that have a variety of Anatomical Classification codes. For example, naproxen can be classified in N2B (analgesic), M1A (antirheumatic), G2X9 (for gynaecological conditions) or S1R (ophthalmologic use). In other words, these products have different formulations and/or specific strengths with different indications and are clearly different products. These products may have different brand names.

Another example of how a substance will be classified in different classes is provided as follows: It is clear that if a class is called "nitrites and nitrates", then this is mainly a substance-based class. However, if this is a subclass in the cardiovascular system, a product that is a nitrite but not for use on the cardiovascular system, will not, under normal circumstances, be allocated the code for "nitrites and nitrates."

Note that some Guideline class descriptions specify some substances as inclusions, e.g., "This group includes..." This does not mean that the class excludes all other products, unless it is clearly stated as such.

C Classification of Products – Plain versus Combination

C1 Classification of plain products

Products containing one active substance are defined as plain. Products containing two or more components belonging to the same therapeutic class are also defined as plain. For example, if there are two corticoids in one product from the same class, it will be considered as plain.

Products containing auxiliary substances intended to

- reduce pain at the site of injection (e.g., antibiotics plus local anaesthetic)
- reduce gastro-intestinal discomfort with the active substance (e.g., acetylsalicylic acid plus glycerine)
- modify untoward effects of a substance (paracetamol plus cysteine)
- increase the stability of the product

are also considered as plain products.

C2 Classification of combination products

Products containing two or more active ingredients from different classes are regarded as combination products. Products containing two or more components of the same therapeutic class are classified as plain.

Separate Anatomical Classification System 3rd or 4th levels have been assigned for some important combination groups, e.g., C9B2 ACE inhibitors/Betablocker combinations.

If there is no specific code for a certain combination of substances, then the indications and use take priority in the normal case. In cases where one or more classes would be possible, the default is to the higher level of the Anatomical hierarchy, unless specified otherwise.

Products sold as kits/combination packs include different tablets or forms with different ingredients. Fixed dose products contain the ingredients in one dosage form.

Products sold as kits containing either separate products or different formulations are classified according to the predominant usage. Generally, systemic formulations take priority over topical. However, each kit must be judged on its own merit.

D Classification of new products

D1 General

The Classification Committee decides if a product can be classified in a class that already exists. If not, then new groups/classes need to be designed to cater for new markets for which these products are indicated. The new product is classified in the most suitable existing class until another new class is agreed upon. If there is a problem with the classification, e.g., companies object, then the Classification Committee should address this issue.

Conditions

A 2nd, 3rd, or 4th level **new class** can be created when the following conditions are fulfilled: when a new substance with an approved indication is launched in one country and a second or similar substance is in pre-registration. This information can be seen in internationally recognized sources like *R&D Focus*, *Pharma Project*, etc. A one-product class will never be created. *See Implementation section below.*

Reasons to Create a new Class

New classes may be created when a current class at 2nd, 3rd, or 4th level needs to be split up as over time new families of products have been introduced, to recognize emerging markets, to reconcile anomalies in the market, or to harmonize with the WHO system.

Use and Re-Use of Classification Codes

The actual classification code does not have any meaning except at the first level (eg A). The sequence of codes does not generally imply any priority or meaning. In some cases a rule is created for a particular area where the order of the classes is important; however any code can be used for any description. In addition, the letter X and the number 9 are usually used for the 'Other' classes.

There can be gaps between codes in a sequence eg A10H can be followed by A10K, ie there is no A10J. This may be because room is being left for classes that may come into operation later but not at the moment. The letters I and O are avoided because of confusion with numbers 1 and 0.

If a code is deleted it is not used again for 3 years; this is to avoid confusion in describing classes by code and to ensure there is not mixed data in datasets created at the time of changeover to the new code structure. This code discontinuity can cause gaps to appear in a code sequence; there is no significance to this for the actual classification.

Codes should not be different to the WHO codes at the third level; in some cases this may exist for historical reasons before harmonisation work started (see Harmonization with WHO).

The valid EphMRA/PBIRG codes are from A to V7.

D2 Procedure

Proposals for new classes (1st, 2nd, 3rd, or 4th level) are presented to the Anatomical Classification Committee by its members and by non-members. New classes can also be recommended by the Committee if it sees the necessity for change because of emerging markets or anomalies in the existing system. If a change is

requested, full definitions should be supplied. In addition, the Committee keeps in close contact with WHO to review proposed changes to their ATC system so as to avoid inadvertent divergence of the two systems.

In order to create a new class within the system, there must be a compelling market need for a new class, and there must be a product with an approved indication launched in at least one country and a second product of a different substance in pre-registration and therefore expected to be launched soon after. Classes may be approved in anticipation of the criteria being fulfilled at the time of implementation of the new class. In other words, more than one substance must be on the market at the time that the new class takes effect, although the class may be approved with one substance already launched and a second expected to be launched. A class will not be created for multiple products of the same substance.

The proposals should be clearly stated and the impact of the change to the system should be outlined. This includes suggested classification of the products affected by a proposed change. The proposal is carefully reviewed by the entire Committee, which consults, as needed, with appropriate involved member companies and sometimes with medical opinion leaders. The Committee reviews the proposed changes with the outside consultants and may solicit alternative suggestions. The purpose is to find out if there is general consensus that the system should be modified and what the changes should be. The responsible Committee member finalizes the proposal. The finalized proposal with background information is sent out to the full EphMRA/PBIRG membership for voting in the second quarter of the year.

Any proposed alteration should be supported by the personnel located in the official headquarter company.

The finalized proposals are sent to the EphMRA and PBIRG members in the early part of the second quarter of the calendar year. The companies vote on these proposals. (See section on Voting.) Special attention is given to those companies who actually have an interest in the new classes. Classes are proposed in anticipation of the criteria being fulfilled at the time of implementation of the new class.

D3 Implementation

The new classes come into effect in the first audit of the following year.

The classes will be created when the majority of the voting companies are in favour of the new proposed classes. If 2/3 of the voting members are in favour of the proposition, then it is fact. If less than 2/3 vote in favour of the new class, then the actively involved box on the voting ballot will be used to determine the outcome. Again, 2/3 of this group must be in favour for the new class to be accepted.

In order for a newly created class to be implemented, there must be two products either on the market or expected in all probability to be on the market within the year of implementation. If a second product does not come to the market within three years, then the class should be reviewed for deletion.

If a new class has been approved but not implemented within three years of the vote due to lack of launched products, then the class should be resubmitted to a vote before implementation.

D4 Voter eligibility

Only full members of EphMRA and PBIRG are eligible to vote. Members have 6 weeks to return votes.

E Changes of classification of existing products

Requests for changes to the classification of individual products are reviewed by the Committee at the quarterly meetings. Requests for change can be made at any time during the year to the local IMS country representative, to a country representative on the Committee, to the Committee member responsible for the target therapeutic class, or directly to the Chairperson of the Committee.

Change of class because of new or changed indication should be supported by the requesting company with substantial documentation. A new brand name or a suffix can be used in order to indicate the new use of an existing product. An approved labeling indicating a new use can also be taken into consideration for change, if the product name has not been changed. If the change request is made by a local affiliate, the Committee may confirm the request with the headquarters company.

Assignments of a product's class can be changed at any point during the product's first twelve months of market life in that country. This time limit may be extended at the discretion of the Committee. Thereafter, requests for change can be made at any point during the year but are effected in the first audit of the year. The major reason for this is to provide audit users with consistent market definitions during the year. Occasionally international products may be changed immediately at the discretion of the committee. The committee will take into consideration the age of the product, the markets in which the product is active, and the classification level. Changes to the coding of new panels may be made during the first two years of the new panel.

Access to the EphMRA/PBIRG Guidelines

The Guidelines to the Anatomical Classification System describe the types of products included in each class. The Guidelines can be obtained through the PBIRG internet site (www.pbirg.com/member services), the EphMRA internet site (www.ephmra.org) or by writing to the General Secretary of EphMRA or the Executive Director of PBIRG.

Bernadette Rogers
General Secretary, EphMRA
Minden House,
351 Mottram Road,
Stalybridge, Cheshire
SK15 2SS
UK
Telephone: [44] 161 304-8262
Fax: [44] 161-304-8104
Email: MrsBRogers@aol.com

Carol Reilly
Executive Director, PBIRG
1758 Allentown Road, Box 209
Lansdale, PA 19446
USA
Telephone: [1] 215 855 5255
Fax: [1] 215 855 5622
Email: creilly@pbirgexec.com

Therapeutic class responsibilities and contact information for Classification Committee members are posted on the EphMRA and PBIRG websites.

Harmonization with WHO

In the 1970s, WHO adapted the EphMRA system for its own needs. This became the system that the WHO calls the Anatomical Therapeutic Chemical system (ATC). At the present time, the two systems are similar but are designed to meet two different goals. The purpose of the WHO ATC is to meet the needs of teaching, clinical trials, health organizations, and governments. The EphMRA/PBIRG Anatomical Classification

system must meet the needs of marketing research and marketing. The WHO ATC classifies substances while the EphMRA/PBIRG Anatomical Classification system classifies products.

In 1991, EphMRA approached the WHO to harmonize the systems because of the increasing use of the WHO system by regulatory bodies. The EphMRA Committee and the WHO have been meeting annually since 1991 in order to align and improve the systems. A high level of harmonization has already been achieved.

Comparison of EphMRA/PBIRG Anatomical Classification with WHO ATC

WHO mainly classifies substances according to the therapeutic or pharmaceutical aspects and in one class only. Particular formulations or strengths can be given separate codes, e.g., clonidine in C2A as antihypertensive agent, N2C as anti-migraine product and S1E as ophthalmic product. EphMRA/PBIRG classifies products, as described earlier in this booklet.

The purposes of classification differ for EphMRA/PBIRG and WHO:

The main purpose of the WHO classification is for international drug utilization research and for adverse drug reaction monitoring. This classification is recommended by WHO for use in international drug research.

The objectives of the WHO system are to:

- develop use of the ATC/DDD system as an international standard for drug utilization studies
- stimulate and influence the practical use of the ATC system by co-operating with researchers in the drug utilization field
- establish DDDs for drugs that have been assigned an ATC code

The EphMRA/PBIRG classification has a primary objective to satisfy the marketing needs of the pharmaceutical companies. Therefore, a direct comparison is sometimes difficult due to the different nature and purpose of the two systems.

The aim of harmonization is to reach a “full” agreement of all mono substances in a given class as listed in the WHO ATC Index , mainly at the 3rd level. Whenever this is not possible, or when harmonization of the 3rd level is too difficult, or when harmonization makes no sense (e.g., C2, R3), the second level will be taken as the reference class.

Harmonization is not a simple adaptation of the two systems. Harmonization is clearly an improvement of the existing systems.

In view of the increasing use of the WHO and EphMRA/PBIRG classification systems by national and international authorities and institutions with different objectives, it must be pointed out that markets can be defined in numerous different ways and the systems are not made and maintained for use outside their primary scope. Within this scope it would be opportune to have a harmonized classification. The main benefit would be that all parties involved in a given topic would use the same or comparable definitions.

In order to help companies compare the two systems, a document has been prepared comparing the two systems to the 3rd level. Contact Bernadette Rogers for a copy of the document.