

GLOSSARY OF TERMS AND GUIDELINES FOR STATISTICAL TABLES BY MEMBER STATES

BACKGROUND

Article 13 of the Council Directive 86/609/EEC obliges the Competent Authorities of the Member States (MS) to collect and make available statistical information on the use of animals in scientific experiments. Article 26 charges the Commission to use this information in order to prepare regular reports for the Council and the European Parliament.

The information submitted by the MS in compliance with Article 13 and 26 will need to be presented in a standardized manner in order to enable meaningful comparisons to be made. In pursuit of this aim, with the agreement of the Competent Authorities, a series of tables has been prepared in order to indicate the categories of information required.

It should be noted that national requirements for data collection may be more detailed than the ones specified in these tables.

The aim of this glossary is to give comprehensive explanations of the table and column headings, with appropriate comments where necessary to assist the completion of the tables.

The relationship between the different tables is indicated below on page 3.

DEFINITIONS

“Animal” unless other qualified, means any live non-human vertebrate, including free-living larval and/or reproducing larval forms, but excluding foetal or embryonic forms (Directive 86/609/EEC Article 2).

“Experiment” means any use of an animal for experimental or other scientific purposes which may cause it pain, suffering, distress or lasting harm, including any course of action intended, or liable, to result in the birth or hatching of an animal in any such condition, but excluding the least painful methods accepted in modern practice (i.e. “humane” methods) of killing or marking an animal; an experiment starts when an animal is first prepared for use and ends when no further observations are to be made for that experiment; the elimination of pain, suffering, distress or lasting harm by the successful use of anaesthesia or analgesia or other methods does not place the use of an animal outside the scope of this definition. Non-experimental, agricultural or clinical veterinary practices are excluded. (Directive 86/609/EEC Article 2).

Note 1 : Under this definition any intervention carried out under terminal anaesthesia is also defined as an experiment.

Note 2 : The killing of an animal by a humane method, for the purpose of obtaining tissues, cells or body fluids is not a procedure under the above definition, if the animal has not been subject to any previous intervention, and therefore need not be included in the table.

Note 3 : Generating a genetically engineered (transgenic/mutant) strain is to be considered as a procedure as covered by Directive 86/609/EEC Article 2 and therefore needs to be included in the statistical tables.

However, breeding of genetically engineered (transgenic/mutant) animals, in itself, would not be a scientific experiment, and need not be included in the statistics.

Note 4 : Marking of fish for stock management purposes is considered as husbandry. It therefore need not be included in the tables. Marking of fish for research purposes does not meet the provisions of Article 2 of the Directive and thus is also excluded from the statistics.

“Humane method of killing” means the killing of an animal with a minimum of physical and mental suffering, depending on the species (Directive 86/609/EEC Article 2) : refer to the guidelines in *Euthanasia of Experimental Animals* (European Commission ISBN 92-827-9694-9).

“Purpose” of animal experiments is defined according to the following broad categories in Directive 86/609/EEC Article 3 :

- (1) the development, manufacture, quality, effectiveness and safety testing of drugs, foodstuffs and other substances or products :
 - (a) for the avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality or their effects in man, animals or plants;
 - (b) for the assessment, detection, regulation or modification of physiological conditions in man, animals or plants;
- (2) the protection of the natural environment in the interests of the health or welfare of man or animal;

and further in Council of Ministers Resolution 86/C 331/02 which, in addition to the categories mentioned above, includes scientific research, education and training and forensic inquiries.

These definitions are further categorized in the statistical tables.

Each of the columns of each table is unique, i.e., once an animal has been entered into one column, it cannot be entered into another column of the same table with the exception of column 1.7, Re-used animals.

SPECIES

Columns 1 of Tables 1 to 7 require figures to be entered according to the animal species used. Both the scientific and common names can be found in table 1. From table 2 onwards only common names have been used.

The category “non-human primates” mentioned in Directive 86/609/EEC has been divided further into prosimians (*Prosimia*), New World monkeys (*ceboidea*), Old World monkeys (*Cercopithecoidea*) and apes (*Hominoidea*). It should also be noted that the category “hamsters” refers to all species of hamster.

RELATIONSHIP BETWEEN THE DIFFERENT TABLES

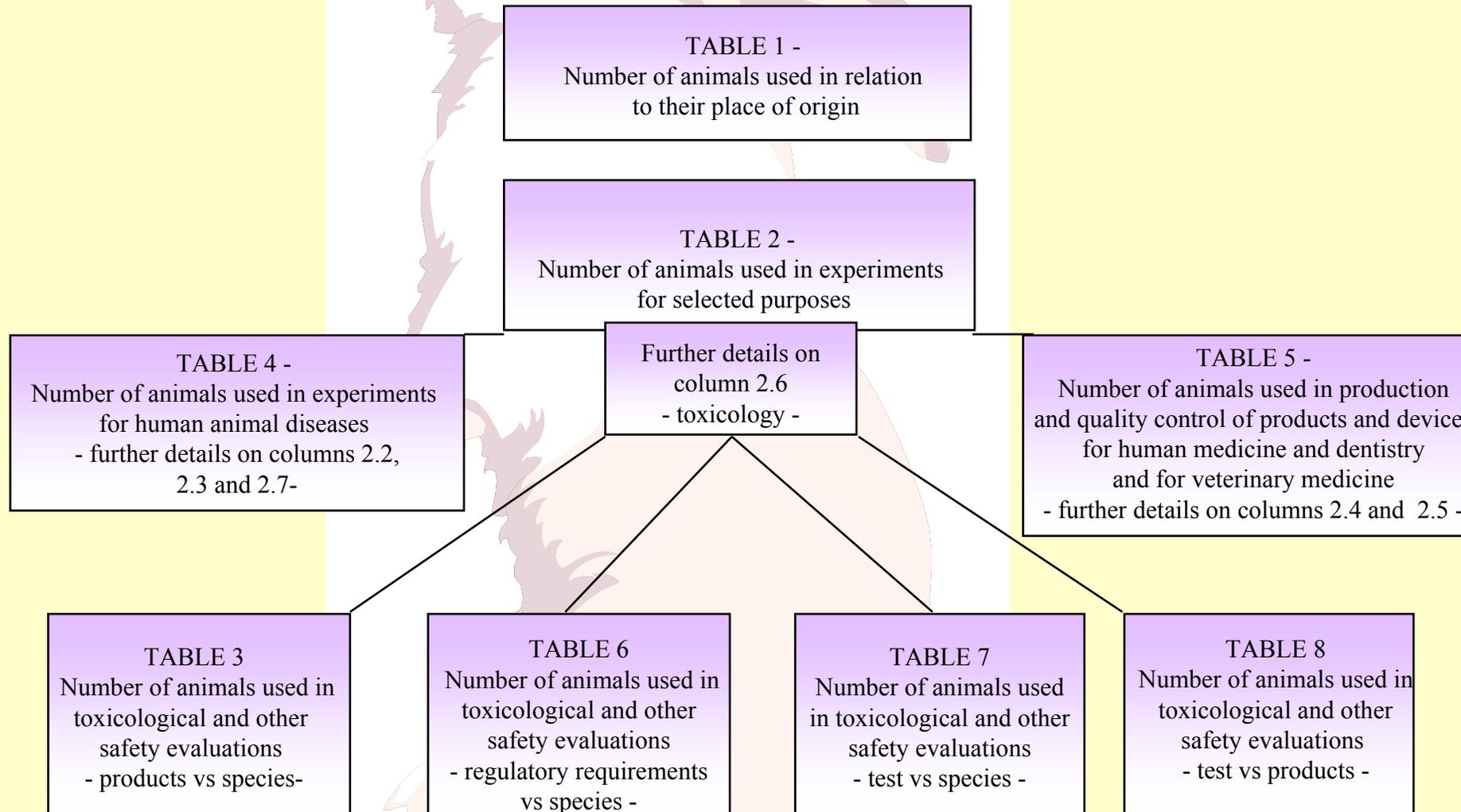


TABLE 1 : ANIMALS USED IN RELATION TO THEIR PLACE OF ORIGIN

Except for column 1.2 “Total” this table refers to species which are covered by Article 21 of Directive 86/609/EEC, namely that only bred animals should normally be used, unless an exemption to this requirement has been granted. However, Article 19(5) of the Directive requires that information on the place of origin be recorded for all animals used.

Column 1.3 **Animals coming from registered breeding or supplying establishments within the reporting country** : establishments registered under the requirements of Article 15 of Directive 86/609/EEC.

Note : At present, registration is carried out on a national basis, and there is no provision for EU-wide registration. Competent Authorities do not have the authority to inquire about the status of breeding and supplying establishments outside of their own country.

Column 1.5 **Animals coming from Member Countries of Council of Europe which are Parties to Convention ETS 123 excluding EC Member States** : this definition does not distinguish between animals that have been bred and animals that have been captured in the wild.

Column 1.6 **Animals coming from other origins** : this definition does not distinguish between animals that have been bred and animals that have been captured in the wild.

Column 1.7 **Re-used animals** : use of the same animal is considered as re-use if the experiments are unrelated or a different animal could have been selected. The figure in this column should **not be added** to the total in column 1.2.

Note : Only the first use should be specified further in the statistical tables and included in the totals.

TABLE 2 : ANIMALS USED IN EXPERIMENTS FOR SELECTED PURPOSES

In cases where an animal has been re-used, only the purpose for which it was first used should be recorded.

Column 2.2 **Biological studies of a fundamental nature** : studies that are designed to add to the store of knowledge about normal and abnormal structure, functioning and behavior of living being; this includes fundamental studies in toxicology.

Note : Further details on animals used in studies of human and animal disease will be entered in Table 4.

Column 2.3 **Research and development of products and devices for human medicine and dentistry and for veterinary medicine (excluding toxicological and other safety evaluation counted in column 2.6)** : applied research which is aimed at the identification, characterization and development of medicinal products, devices, biological and biotechnological products, e.g. vaccines, sera, biological mediators, and any other substances that could, alone or in combination with other substances, potentially be used for curative, palliative, prophylactic or prosthetic purposes in humans and animals. This will include pharmacokinetic and pharmacodynamic studies, studies of mechanisms of action and potential therapeutic activity, studies of possible mechanisms of toxicity and studies of other biological properties. It will also include studies aimed at developing new surgical methods or improving existing ones.

This column will **not include** routine toxicity testing and will **not include** animals used in routine production, quality control, toxicological and other safety evaluation processes, which are covered by columns 2.4 and 2.6.

Column 2.4 **Production and quality control of products and devices for human medicine and dentistry** : this column includes animals used for the routine production of monoclonal and polyclonal antibodies and other biological material used routinely in human medicine and dentistry as referred to in the column 2.3 heading, including products used as diagnostic reagents which are not covered in column 2.7. It also includes animals used in the testing of purity, stability, efficacy, potency and other quality control parameters of the final product and its constituents and any controls carried out during the manufacturing process for registration purposes, to satisfy any other national or international regulatory requirements or to satisfy the in-house policy of the manufacturer.

Note that this column does **not include** animals which have been humanely killed, without being subject to any previous intervention, prior to the removal of organs, tissues, cells or blood. It will not include animals used in routine toxicological and other safety evaluation processes carried out for regulatory or non-regulatory purposes.

Column 2.5 **Production and quality control of products and devices for veterinary medicine** : this column includes animals used for the routine production of monoclonal and polyclonal antibodies and other biological material used routinely in veterinary medicine as referred to in column 2.4, including products used as diagnostic reagents which are not covered in column 2.7. It also includes animals, used in the testing of purity, stability, efficacy, potency and other quality control parameters of the final product and its constituents and any controls carried out during the manufacturing process for registration purposes, to satisfy any other national or international regulatory requirements or to satisfy the in-house policy of the manufacturer.

Note that this column does **not include** animals which have been humanely killed, without being subjected to any previous intervention, prior to the removal of organs, tissues, cells or blood. It will not include animals used in routine toxicological and other safety evaluation processes carried out for regulatory or non-regulatory purposes.

Note : A further breakdown of these figures is required in Table 5 to indicate which procedures were carried out to comply with regulatory requirements.

Column 2.6 **Toxicological and other safety evaluation (including safety evaluation of products and devices for human medicine and dentistry and veterinary medicine)** : studies carried out on any product or substance to determine its potential to cause any dangerous or undesirable effects in humans or animals as a result of its intended or abnormal use, manufacture or as a potential or actual contaminant in the environment.

Note 1 : Pharmacodynamic/kinetic studies should **not be included** here, but in column 2.3, as appropriate.

Note 2 : A further breakdown of these figures is required in Tables 3,6,7 and 8 to indicate the types of products tested, types of tests carried out and compliance with regulatory requirements.

Column 2.7 **Diagnosis of disease** : all animals used in procedures for the diagnosis of human or animal disease including diagnosis of suspected poisoning **excluding** animals used in the research, development, manufacture and quality control of products used for diagnosis purposes. These are covered in columns 2.4 and 2.5.

Column 2.8 **Education and training** : animals used in education at all levels and also animals used for the training of laboratory personnel and for the maintenance and development of surgical skills.

This column does **not include** animals used in research projects carried out as part of a course of study. These animals should be entered into column 2.2.

Column 2.9 **Other** : includes animals used for the production and maintenance of infectious agents, vectors and neoplasms and animals used for the production of monoclonal and polyclonal antibodies and other biological material, insofar as these are not used for the purposes defined in any other column of Table 2.

Note : The purpose of studies involving antibody products needs to be carefully established, because any column of Table 2 could apply.

TABLE 3 : ANIMALS USED IN TOXICOLOGICAL AND SAFETY EVALUATIONS

This table requires a further breakdown of the figures entered in column 2.6 of Table 2 (see above), in order to classify animal use by the types of substances that have been studied. Columns 3.2-3.8 will include animals used in studies to define potential toxicity of substances in the course of their production, normal and abnormal usage and also to define the potential danger of these substances and any related by-products as environmental contaminants.

Column 3.2 **Products/substances or devices for human medicine and dentistry and for veterinary medicine** : medicinal products, devices, biological and biotechnological products, e.g. vaccines, sera, biological mediators, and any other substances that could, alone or in combination with other substances, potentially be used for diagnostic, curative, palliative, prophylactic or prosthetic purposes in humans and in animals.

Column 3.3 **Products/substances used or intended to be used mainly in agriculture** : e.g. pesticides, fertilizers, herbicides.

Column 3.4 **Products/substances used or intended to be used mainly in industry** : e.g. raw materials, intermediate products, solvents, reagents, catalysts, purifiers used in bulk production and in other industrial processes.

Column 3.5 **Products/substances used or intended to be used mainly in the household** : products used for all domestic purposes, **excluding** food products and products used for cosmetic purposes, purposes of personal hygiene and medical purposes.

Column 3.6 **Products/substances used or intended to be used mainly as cosmetic or toiletries** : “any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition” (Council Directive 93/35/EEC, Article 1), or any product/substance or preparation intended to have a primary use as an ingredient of a cosmetic formulation.

Column 3.7 **Products/substances used or intended to be mainly as additives in food for human consumption** : any substance, including novel food, e.g. bioprotein, when added to food materials to enhance their taste, colour, handling/processing or keeping properties, where the final product will primarily be consumed by humans.

Column 3.8 **Products/substances used or intended to be used mainly as additives in food for animal consumption** : any substance, including novel food, e.g. bioprotein, when added to food materials to enhance their taste, colour, handling/processing or keeping properties, where the final product will primarily be consumed by domestic or farm animals. It also includes products to increase yield from animals (but **not** products used to treat or to prevent pathological conditions in these animals).

Note : This would **not include** studies on the pharmacological or therapeutic effects of nicotine or other alkaloids derived from the tobacco plant.

Column 3.9 **Potential or actual contaminants in the general environment which do not appear in other columns** : any substances, effluent or by-product that does not arise during the manufacture of products defined in columns 3.2-3.8 and that is a potential contaminant of the environment.

Column 3.10 **Other toxicological or safety evaluations** : studies concerning any substances not elsewhere defined in this table.

TABLE 4 : ANIMALS USED IN EXPERIMENTS FOR STUDIES ON HUMAN AND ANIMAL DISEASES

The numbers entered into this table are a subgroup of some of the numbers entered into columns 2.2, 2.3 and 2.7 of Table 2.

Column 4.2 **Human cardiovascular diseases** : includes animals used in research studies on the pathogenesis, diagnosis and treatment of disorders affecting the human cardiovascular system, respectively, apart from malignancies.

Column 4.3 **Human nervous and mental disorders** : includes animals used in research studies on the pathogenesis, diagnosis and treatment of disorders affecting the human nervous system and mental disorders in humans, apart from malignancies.

Column 4.4 **Human cancer (excluding evaluations of carcinogenic hazards or risks)** : includes animals used in research studies on the pathogenesis, diagnosis and treatment of malignant disorders in humans (human cancer), but does **not include** animals used in other carcinogenicity studies.

Column 4.5 **Other human diseases** : includes animals used in research studies of the pathogenesis, diagnosis and treatment of any disease state in humans that is not covered by the definitions in columns 4.2, 4.3 and 4.4.

Column 4.6 **Studies specific to animal diseases** : includes animals used in research studies of the pathogenesis, diagnosis and treatment of any disease state, including malignancies, in animals.

TABLE 5 : ANIMALS USED IN PRODUCTION AND QUALITY CONTROL OF PRODUCTS AND DEVICES FOR HUMAN MEDICINE, DENTISTRY AND FOR VETERINARY MEDICINE

This table requires a further breakdown of figures entered into columns 2.4 and 2.5 of Table 2 in order to indicate how many of the animals have been used to satisfy regulatory requirements.

Column 5.2 **National legislation specific to a single EC Member State** : animals used to satisfy regulations imposed at a national level only by any single EC Member State, including the Member State where the experiment is carried out.

Column 5.3 **EC legislation including European Pharmacopoeia (requirements)** : animals used to satisfy the requirements of EU legislation and/or European Pharmacopoeia requirements.

Column 5.4 **Member Country of Council of Europe (but not EC) legislation** : animals used to satisfy regulatory requirements of any third party state in the Council of Europe which is not a Member State of EU, whose regulations extend beyond the EU legislation and/or European Pharmacopoeia requirements.

Column 5.5 **Other legislation** : animals used to satisfy regulatory requirements not covered by columns 5.2, 5.3 and 5.4, e.g., regulations of United States Food and Drug Administration (FDA).

Column 5.6 **Any combination of 5.2/ 5.3/ 5.4/ 5.5** : animals used in any test that satisfies two or more out of the following : national, EU, Member Country of Council of Europe or other legislation or European Pharmacopoeia requirements.

Column 5.7 **No regulatory requirements** : animals used in procedures relating only to the in-house requirements of the manufacturer.

TABLE 6 : ANIMALS USED IN TOXICOLOGICAL AND OTHER SAFETY EVALUATIONS

This table requires a further breakdown of figures entered into column 2.6 of Table 2 in order to indicate how many of the animals have been used to satisfy regulatory requirements. The classification of regulatory requirements in columns 6.2 - 6.7 is as defined for columns 5.2-5.7 of Table 5 (see above).

Column 6.3 For human and veterinary medicinal products, this includes the legislation laid down in Directives 75/318/EEC and 81/851/EEC and the Guidelines published by the European Commission in “The rules governing medicinal products in the European Union” (Office for Official Publications of the European Communities, Luxembourg).

TABLES 7 AND 8 : ANIMALS USED IN TOXICOLOGICAL AND OTHER SAFETY EVALUATIONS

These tables require a breakdown of figures entered in column 2.6 of Table 2 in order to indicate the types of toxicity tests performed. These are further classified by species used (Table 7; same species listing as in Tables 1 - 6), and by categories of products tested (Table 8, using the product categories defined in Table 3).

Types of test in Tables 7 and 8 :

Columns 7.2 and 8.2. **Acute (14 days) and sub-acute (28 days) toxicity testing (including limit test)**

Sub-columns 7.2.1 and 8.2.1 **LD50, LC50** : classical method encompassing defined minimum numbers of animals and several single dose levels which will encompass the LD50 (lethal dose) (e.g. Directive 67/548/EEC, Annex V, method B.1, B.2, B.3, OECD TG 401, 402, 403).

Sub-column 7.2.2 and 8.2.2 **Other lethal methods** : alternative methods with a lethal endpoint that allow prediction of the LD50, e.g. approximate lethal dose, up-and-down method, acute toxic class method, (e.g. Directive 67/548/EEC, Annex V, method B.1tris, OECD TG 423).

Sub-columns 7.2.3 and 8.2.3 **Non lethal clinical signs methods** : observation of non-lethal responses that effect general well-being after a single limit dose or repeated dose, estimation of ED50 values (effective dose), fixed dose procedure (e.g. Directive 67/548/EEC, Annex V, method B.1bis, B.7, B.8, B.9, OECD TG 407, 410, 420)

Columns 7.3 and 8.3 **Skin irritation** : topical application of a single dose to the shaved skin, such as Draize skin test (e.g. Directive 67/548/EEC Annex V method B.4, OECD TG 404)

Columns 7.4. and 8.4 **Skin sensitization** : topical or intradermal application of the test substance to the skin, followed by application of a challenge dose, e.g., Draize skin sensitization test, open epicutaneous test, Buehler test, Freund's Complete Adjuvant test, optimization test, split adjuvant test, guinea pig maximization test, local lymph node assay, mouse ear swelling test, vitamin A enhancement test (e.g. Directive 67/548/EEC, Annex V, method B.6, OECD TG 406)

Columns 7.5 and 8.5 **Eye irritation** : topical application of a single dose to the eye, e.g. Draize eye test (e.g. Directive 67/548/EEC Annex V method B.5, OECD TG 405)

Columns 7.6 and 8.6 **Sub-chronic and chronic toxicity** : repeated dose medium and long term studies aimed at identifying adverse effects arising from prolonged exposure by various routes, target organs or site of action, risk assessment (e.g. Directive 67/548/EEC, Annex V, method B.26, B.27, B.28, B.29, B.30, B.33; OECD TG 408, 409, 411, 413, 452).

Columns 7.7 and 8.7 **Carcinogenicity** : long-term continuous exposure studies (18-36 months) to monitor tumor development; studies on tumor promotion, such as two-stage skin cancer and hepatic cancer assays (e.g. Directive 67/548/EEC, Annex V, method B.32, B.33, OECD TG 451)

Columns 7.8 and 8.8 **Developmental toxicity** : studies carried out in pregnant animals to determine the potential of a substance to cause fetal abnormalities, embryotoxicity or otherwise affect fetal development (e.g. OECD TG 414)

Columns 7.9 and 8.9 **Mutagenicity** : studies to determine the potential of a substance to damage DNA, e.g. mouse spot test, transgenic mouse assay, rodent micronucleus assay, dominant lethal assay, unscheduled DNA synthesis, sister chromatid exchange, DNA binding in target organs, liver focus assay in rats (e.g. Directive 67/548/EEC, Annex V, method B.11, B.12, B.23, B.24, B.25; OECD TG 474, 478)

Columns 7.10 and 8.10 **Reproductive toxicity** : studies to determine the potential of a substance to affect the fertility and fecundity of males and females, e.g. single and multi-generation reproduction test (e.g. Directive 67/548/EEC, Annex V, method B.22, B.31, B.34, B.35; OECD TG 415, 416)

Columns 7.11 and 8.11 **Toxicity to aquatic vertebrates not included in other columns** : e.g. Directive 67/548/EEC, Annex V, method C.1

Columns 7.12 and 8.12 **Other** : e.g. studies of the effects of a substance in defined target organs and systems, studies of behavioral effects, of percutaneous absorption, of toxicokinetics (e.g. Directive 67/548/EEC, Annex V, method B.36., B.37., B.38; OECD TG 417).

Note : No separate classification is given for inhalation studies and pharmacokinetic/metabolic studies, although these are given separate treatment, e.g., in the Council Recommendation 83/571/EEC concerning tests relating to the placing on the market of proprietary medicinal products.