The amendments made with the “Regulation Amending the Regulation Regarding the Packaging and Labeling of Medicinal Products for Human Use” published on the Official Gazette dated 01.02.2008, with No. 26775, have been implemented.

Regulation Regarding the Packaging and Labeling of Medicinal Products for Human Use

SECTION ONE
Objective, Scope, Legal Basis and Definitions

Objective
Article 1- The objective of this Regulation is to set forth the procedures and principles regarding the information that must be contained on the label and in the package as well as the package insert to ensure the identification and correct use of medicinal products for human use in terms of the health and safety of the persons who will use the registered/permitted medicinal products for human use.

Scope
Article 2- This Regulation shall comprise the minimum compulsory information and conditions that must be contained on the label, packaging and package inserts of medicinal products for human use and real persons or legal entities that have applied for registration/permit and/or who have been granted a registration/permit.

Legal Basis
Article 3- This Regulation has been prepared on the basis of Law No. 1262 on Pharmaceutical and Medicinal Preparations, dated 14/05/1928, clause (k) of paragraph one in article 3 of Principal Law No. 3359 on Health Services and article 43 of Decree Law No. 181 on the Organization and Duties of the Ministry of Health;

In line with Directive 2001/83/EC on medicinal products for human use, for the purpose of ensuring harmonization with the relevant legislation of the European Union regarding medicinal products for human use.

Definitions
Article 4- For the purposes of this Regulation, the following definitions shall apply:

Ministry: The Ministry of Health,
Medicinal Product for Human Use/Product: Any natural and/or synthetic-based active substance or combination of substances administered to human beings with a view to treating and/or preventing a disease, making a diagnosis or restoring, correcting or modifying physiological functions,
International Non-proprietary Name/INN: The international name of an active substance, accepted or suggested by the World Health Organization, that does not have international proprietorship and should not be used in brand registration in line with the rules of the World Health Organization,
Common name: The common or scientific name of the product which will prevent it from being confused,
Name of the medicinal product for human use: The common or scientific name which will prevent the confusion of the product with INN or the common name, is an invented name and is accepted by the Ministry and is taken as basis in registration/permit.

Unit amount of the medicinal product for human use: The quantitative amounts of the active substance/substances contained in the unit dose, unit volume or unit weight of the product, depending on the pharmaceutical form.

Pharmaceutical form: The presentation form of the medicinal product manufactured according to its purpose of use.

Outer package: The package into which the immediate package is placed.

Immediate package: The container in which the product is placed or the form of package directly in contact with the product.

Labeling: Information on the immediate or outer package.

Package insert: Written information presented with the product, prepared for the users.

Summary of Product Characteristics (SPC): The summary of the product characteristics contained in the medicinal product’s registration dossier.

Active substance: The pharmacological active substances used in medicinal products for human use.

Excipient: Substances included into the composition of the product, aside from the active substances/substances.

Manufacturer: Real person or legal entity releasing the product to enable it to be placed on the market.

Data matrix: Data matrix type two-dimensional barcode.

Legible information: Descriptive content information written under or near the identifier for the purpose of demonstrating the content relating to the barcode or data matrix to the users.

SECTION TWO
Outer Package, Immediate Package and Package Insert

Outer Package

Article 5 - The following shall appear on the outer package or, in case it is not included on the outer package, the immediate package of the product:

a) The name of the medicinal products for human use, the unit dose, pharmaceutical form and whether they are intended for babies, children or adults, where necessary, shall be indicated. In case the product contains up to three active substances, the INN, or in the absence of the INN, its common name shall be used.

b) The unit amounts or administration routes and the weight or volume amounts according to the pharmaceutical form of the active substances indicated as INN or common name will be specified.

c) The units such as the number of tablets, ampoules, bottles contained in the package shall be indicated numerically as unit amount; whereas the active substances in the pharmaceutical form which cannot be regarded as net content, shall be indicated as volume or weight or dose number; excipients such as coloring matters, preservatives, antioxidants, flavoring substances and alcohol will be indicated in name:

1) The net amount shall be indicated in aerosols; the number of doses and the dose per spray shall be specified for metered-dose inhalers.

2) The amount of substances in large-volume parenteral solutions shall be indicated in millimole.

3) Where possible, also the milligram or gram values corresponding to the international unit (IU) shall be written.
4) The number of drops per milliliter shall be indicated for products administered orally in drops.
5) The net content in grams shall be indicated for semi-solid pharmaceutical forms such as ointments and creams.
6) In packages used via a beaker and which contain a beaker, the formula shall be indicated as dose per beaker ad the weight or volume of the amount of product per beaker shall be indicated.
7) The formula of the product in the form of ampoules, vials and single-dose injectors shall be indicated as the amount per millimeter or in the whole package. The same rule shall apply for injectable products in powder or concentration and used upon being dissolved in a solvent.

d) The excipients known to have an evident effect and are indicated on the guidance specified in paragraph one of article 19 of this Regulation shall be presented as a list. However, if the product is injectable or is locally applicable or is an ocular preparation, all excipients shall be indicated.

e) The method and, if necessary, the route of administration shall be indicated. The required space shall be left for indicating the prescription dose.

f) The special warning stating: “Keep in its package, in a place that cannot be seen and reached by children”.

g) Where available, other special warnings relating to the product shall be indicated.

h) The storage conditions, and if any, the special storage conditions of the product will be indicated.

i) Special warning relating to the disposal of unused products or wastes of products and, where necessary, the appropriate collection system shall be indicated.

j) The symbol of recyclable package, the number and abbreviation of the type of package shall be indicated on the packages as per the Regulation on Packaging and Package Wastes published on the Official Gazette dated 24/06/2007, with No. 26562. Except for the products mentioned under the title of Radiopharmaceuticals in this regulation, the management of the wastes of immediate, outer and transportation packages which are not classified as medical and hazardous wastes shall be conducted within the scope of the referred regulation.

k) The name and address of the registration/permit holder shall be indicated on the package of the product. If desired, also the name of the company marketing the product that has been authorized to represent the registration/permit holder shall be indicated.

l) The name and address of the manufacturer shall be indicated.

m) The registration/permit number of the product will be indicated.

n) The batch number shall be indicated in the secondary identifier information and legible information of the data matrix.

o) The expiry date shall be indicated clearly in accordance with the size and characteristics of the immediate package, with the month written in numbers or letters and the year only in numbers,

p) In case it is a product which is used for self-medication purposes, relevant instructions for the users shall be provided.

q) The warnings: “Do not purchase packages that have been cut or opened”, “Read the package insert before use”, “Consult your doctor if any undesirable effects appear” as well as other warnings issued by the Ministry shall be included.

r) A statement indicating whether the product is or is not subjected to a prescription shall be included.
s) A secondary identifier named data matrix and legible information relating to the content of the data matrix shall be provided next to it for the purpose of ensuring the traceability of products. Registration/permit holders shall apply the data matrix and the legible information relating to its content in a manner so as to be read by two-dimensional barcode readers widely available in the market, within the framework of the standards specified in the barcode implementation guidance to be issued in relation with this regulation. The data matrix shall be included on the packages of promotional samples, hospital-packed products, prescription or non-prescription drugs, borderline products subjected to reimbursement and medical nutritional products.

t) The barcode of the product shall be included.

Immediate Package

Article 6 - Except for the particulars indicated in clauses (a) and (b) of paragraph two of this article and clauses (p), (q), (r) and (t) of paragraph one of article 5 of this Regulation, immediate packages shall bear the properties and information indicated in article 5 of this Regulation.

Provided that conformance is achieved with paragraph one of this article, the following shall apply in particular:

a) In immediate packages in the form of blisters;
   1) The name of the product as laid down in clause (a) of paragraph one of article 5 in the Regulation,
   2) The name or emblem of the registration/permit holder,
   3) The expiry date indicated clearly in accordance with the size and characteristics of the immediate package, with the month written in numbers or letters and the year only in numbers,
   4) The batch number.

b) In immediate packages which are too small to contain the properties and information designated for labeling in article 5 of the regulation, the following shall be included;
   1) Where possible, the name or emblem of the registration/permit holder,
   2) The name of the product; where necessary, the dose and route of administration,
   3) The expiry date written clearly as month and year,
   4) Batch number,
   5) Weight, volume or unit unit/amount content,
   6) Route of administration.

The current packages of products with no outer packages, shall comply with article 5 of the Regulation.

The batch number shall be included in the immediate packages.

See-through Transparent Outer Packages

Article 7 – It is not mandatory to apply labeling on see-through transparent outer packages. However, in this case, all of the information to be contained on the outer package shall be included on the immediate package.

Package Insert

Article 8- The package insert shall be prepared in accordance with the SPC of the product, in a manner that is understandable by the user and will fulfill the following:

a) For the purpose of identifying the product;
   1) The name of the medicinal products for human use, the unit dose, pharmaceutical form and, whether they are intended for babies, children or adults, where necessary, shall be
indicated; if the product contains only one active substance and bears an invented name, it shall be used along with its common name.

2) The unit amounts or route of administration and the weight or volume amounts according to the pharmaceutical forms of all active substances indicated with their INN or common name shall be indicated.

3) The units such as the number of tablets, ampoules, bottles contained in the package shall be indicated numerically as unit amount; whereas the active substances in the pharmaceutical form which cannot be regarded as net content shall be indicated as volume or weight or dose number.

4) The therapeutic group or the type of efficiency shall be indicated in terms which are to be easily understood by the patients.

5) The name and address of the registration holder and manufacturer of the product will be provided.

b) The areas where it is used in treatment (the therapeutic indications) shall be indicated.

c) The following shall be indicated as relevant information before using the product:

1) Cases where it should not be used,
2) Descriptions relating to its use,
3) Interactions with other medicinal products for human use or other interaction types that may influence the effect of the medicinal product for human use (e.g.; alcohol, tobacco, food),
4) Warnings relating to specific patient groups such as children, pregnant or breastfeeding women, elderly and people in special pathological conditions,

5) Where available, the effect of the product on driving vehicles and using machinery,
6) Special warnings relating to excipients that have are important in terms of the safe and effective use of the product,

d) The following shall be provided as general and relevant information for the correct use of the product;

1) The amount to be used (Dosage),
2) The method and, where necessary, the route of administration,
3) The administration frequency of the product upon indicating also that it is to be used where necessary or the right time when it is to be used,

e) The following shall be indicated in relation with the structure of the product;

1) Where necessary, the time when the treatment should be interrupted, the duration of the treatment,
2) The symptoms to be observed, the measures to be adopted and the relevant emergency interventions in case of overdose,
3) The steps to be taken in case one dose or more doses are not taken,
4) Where necessary, information regarding the risks that may arise in case of interruption of the use of the product.

f) The undesired effects to arise during the normal use of the product and the measures to be adopted in case of such a condition; and information on the need to consult one’s doctor or pharmacist in case of any undesired effect not indicated in the package insert.

g) The following shall be specified along with the statement emphasizing that the expiry date in indicated on the label;

1) Warning indicating that it should not be used after this date,
2) The storage conditions,
3) Where necessary, warning against an evident degradation/variation in the product,
4) The full qualitative composition upon using the common names for the presentation of each medicinal product for human use (in the active substances and excipients) and the quantitative composition in the active substances,
5) The pharmaceutical form and the content as the weight, volume or dosage unit for each product presentation,
6) The name and address of the manufacturer.

h) The date when the package insert was last updated shall be provided.

Upon considering that the therapeutic indications of the product and some information relating to the product may give rise to severe drawbacks for the patients, the Ministry may decide to not include it into the package insert.

**Article 9** - The inclusion in the packaging of all products of a package insert shall be obligatory unless all the information required by Articles 5 and 6 is directly conveyed on the outer packaging or on the immediate packaging.

**Terms for Labeling**

**Article 9** – The information indicated in articles 5, 6 and 8 of this Regulation shall be legible, clearly understandable and indelible.

**Symbols and Other Information**

**Article 10** – The outer package and the package insert may include symbols describing the information indicated in articles 5 and 8 of this Regulation and other information which are beneficial for the users and are in compliance with the SPC of the product, provided that they are encouraging and are not promotional in nature.

The particulars relating to the symbols and information mentioned in paragraph one of this article shall be arranged with the guidance indicated in paragraph one of article 19 of the Regulation.

**Information on Promotional Samples**

**Article 11** – The following shall apply for the products to be used for promotion in accordance with the provisions of the Regulation Regarding the Promotional Activities of Medicinal Products for Human Use, published on the Official Gazette dated 23/10/2003, with No. 25268.

a) They have to comply with the terms indicated in this Regulation. However, no barcodes shall be included into the packages of these products; only the data matrix and the legible information relating to the content of the data matrix shall be clearly provided.
b) They shall contain a reduced amount. However, this term shall not be sought in promotion samples of the products which cannot be reduced due to technical reasons.

**Solvents**

**Article 12** – Also the products which are placed on the market as a solvent alone or to be used with another medicinal product for human use shall comply with the provisions of this Regulation. Regarding solvents which are presented in the same package with any medicinal product for human use, the name and/or formula of the solvent and its net content shall be indicated on the outer package and the package insert.

**Products with a Restricted Period of Use**

**Article 13** – The duration of use and storage conditions of products with a restricted period of use upon being dissolved, diluted or opened shall be separately indicated on the package.

**Other Conditions Relating to Packages**
Article 14 – In case all the information requested in articles 8 and 10 of this Regulation are not indicated on the immediate or outer package of the product, the presence of the package insert shall be mandatory. Where necessary, also the materials for using the product shall be provided along with the package insert.

Sterile products shall be marked as “sterile” and apyrogenous products shall be marked as “apyrogenous” on the outer and immediate packages and the package insert.

For the purpose of preventing confusion and mistakes, an evident difference in color and/or height shall be ensured at relevant places in the packages of products which are similar in terms of pharmaceutical form and presentation and have a different unit dose.

The information relating to the outer and immediate packages and the package insert shall be in Turkish for the market placement of the product. However, where necessary and if desired, in addition to the use of Turkish in the outer and immediate packages and the package insert, also one of the official languages of the EU member states and the one of the official languages of the other countries may be used.

However, in case the outer and immediate packages cannot be prepared in Turkish, the package to be prepared in Turkish in accordance with article 8 of this Regulation shall be included at all means and the label bearing the information indicated in article 5 of this Regulation shall be adhered on a suitable place so as not to come off.

Application

Article 15 – The following shall be conducted in the applications for registration/permit;

a) Two samples or drafts of the outer and immediate package and the draft package insert prepared for the placement of the product in the market shall be submitted to the Ministry.

b) In case the outer package, label and the package insert of the product is not compliant with the information indicated on this Regulation or the SPC, the Ministry shall reject the application for registration/permit.

c) The variations planned to be made on the outer package, label or the package insert and are included into the scope of this Regulation even though they are not encompassed by the SPC, shall be presented to the Ministry. In case the Ministry does not grant approval within ninety (90) days as of the application date, the applicant may implement the variation.

d) The Ministry’s rejection of the request for registration/permit in accordance with clause (b) or a variation to be made on the outer package, label or package insert according to clause (c) shall not relieve the manufacturer or, where necessary, the registration/permit holder from his/her legal responsibilities.

e) Product applications for outer package, label and package insert in compliance with this Regulation shall not be rejected.

In registered/permitted products, the variations planned to be made on the outer package, label or the package insert and are included into the scope of this Regulation even though they are not encompassed by the SPC shall be presented to the Ministry. In case the Ministry does not grant approval within ninety (90) days as of the application date, the applicant may implement the variation.

Distribution

Article 16 – No matter how it is distributed (such as retail, wholesale, tenders) each product shall comply with the provisions of this Regulation. However, some additional information in acquisitions to be made by public healthcare institutes and institutions may be used in labeling, provided that they are not in violation of this Regulation.
Registration/permit holders shall use transportation packages during the shipment of more than one product so as to ensure product reliability. The transportation packages may be in the form of packs, parcels, boxes or bundles and may be placed inside one another. The amounts to be contained by transportation packages shall be designated at reasonable levels so as to ensure that they may be carried until the final destination without being opened during the sale.

On the transportation packages, there shall always be an identifier containing the information defining the transportation package or an identifier containing all the data matrix information of the products inside the transportation package. The identifiers to be placed on the transportation package shall be applied as indicated in the barcode implementation guidance to be issued in relation with this regulation.

SECTION THREE
Radiopharmaceuticals

Article 17- The package of the medicinal products for human use containing radionuclides shall be labeled in accordance with the regulation regarding the Turkish Atomic Energy Agency and other relevant international legislations.

The label on the shielding shall comply with article 5 of this Regulation, except for the provisions set forth in clauses (f), (i), (p) and (r) in paragraph one of article 5. Furthermore, the label on the shielding shall fully describe all codings. The radioactivity sign, the amount of radioactivity per dose or per vial, specific activities, the calibration date (time and the time zone), the number of capsules, or, for liquids, the amount of milliliters in the container shall be indicated.

The vial shall be labeled with the following information:
   a) The name or code of the medicinal product for human use, including the name or chemical of the radionuclide and its chemical symbol,
   b) The batch identification and expiry date,
   c) The international symbol for radioactivity,
   d) The name and address of the manufacturer,
   e) The particulars specified in paragraph two of this article.

Package Insert of Radiopharmaceuticals

Article 18- It is mandatory to include a detailed package insert into the package of radiopharmaceuticals, radionuclide generators, radionuclide kits or radionuclide precursors.

The package insert shall be prepared in compliance with article 8 of this Regulation. This brochure shall also contain any special measures to be adopted by the administrator and the patient during the preparation and administration of the product and the warnings for the adequate disposal of unused parts or packages.

SECTION FOUR
Miscellaneous and Final Provisions

Guidance

Article 19- The Ministry shall publish in the form of a guidance the general principles to be complied with where necessary and in relation with the following;
   a) The preparation of warnings for some product categories,
b) The preparation of special information for users in case of products to be used for self-medication purposes,

c) The comprehensibility of the Package and Label information,

d) The identification methods, the content of identifiers to be included on outer packages and transportation packages and the reliability of the product,

e) The list of all excipients that should be indicated on the label and the manner in which they will be indicated.

The Ministry may issue supplementary guidelines or notifications relating to the enforcement of the Regulation for conditions not indicated in this Regulation and where deemed necessary.

Penalty Provisions and Precautions

Article 20 – For those who fail to act in accordance with the provisions of this Regulation, Law No. 1262 on Pharmaceutical and Medicinal Preparations, dated 14/05/1928 and, according to the characteristics and nature of their acts, the provisions of Turkish Penal Code, with No. 5237, dated 26/09/2004 shall apply.

Furthermore, in case of detection of violation of the provisions of this Regulation, the measures and sanctions envisaged by the Regulation Regarding the Registration of Medicinal Products for Human Use published on the Official Gazette dated 19/01/2005, with No. 25705 shall apply.

Revoked Regulation

Article 21 – The Regulation Regarding the Packaging and Labeling of Pharmaceuticals for Human Use and Medicinal Preparations published on the Official Gazette dated 24/04/1991, with No. 20851, has been revoked.

Temporary Article 1 – The packages and package inserts of the current medicinal products for human use which have been registered/permited before the enforcement of this Regulation and of medicinal products for human use for which a registration/permit application has been made, shall become compliant to the provisions of this Regulation latest by 31/12/2007.

The applications to be made for the purpose of evaluating the package inserts encompassed by this Regulation shall be accepted by the Ministry as of the date this Regulation is published on the Official Gazette.

(The validity of this article has been extended to 01/07/2009 for original products and 31/12/2009 for generic products with the “Regulation Amending the Regulation Regarding the Packaging and Labeling of Medicinal Products for Human Use” published on the Official Gazette dated 01/02/2008, with No. 26775.)

Temporary Article 2 – Data matrixes shall be added to pharmaceutical packages as of the publication date of this Regulation by 01/01/2009. It shall be mandatory for all products to have a data matrix after this date and the sale of products manufactured without a data matrix before this date and currently available in the market will be allowed until 31/12/2009.

Temporary Article 3 – Upon the enforcement of this Regulation, in the applications to be made by registration/permit holders for outer packages of registered products that need to be renewed, the notification of the Ministry by the date 01/01/2009 that only the price cuttings have been removed and the data matrixes and legible information have been included shall be regarded as sufficient and there will not be the need for any further approval and the
package updates within this scope shall not be evaluated as variations by the date 01/01/2009. However, it will be necessary to make a variation application for updates to be made after this date. In case package updates contain a change aside from the removal of the price tag and the implementation of data matrix, a variation application shall be made.

Entry into Force
Article 22 – This Regulation shall enter into force on 30/12/2005.

Execution
Article 23 – The provisions of this Regulation shall be executed by the Minister of Health.