K oznámeniu č. 297/2004 Z. z.

EUROPEAN AGREEMENT
ON THE EXCHANGE OF BLOOD-GROUPING REAGENTS

The signatory governments of the member States of the Council of Europe,

Considering that blood-grouping reagents are not available in unlimited quantities;

Considering that it is most desirable that member countries, in a spirit of European solidarity, should assist one another in the supply of these blood-grouping reagents, should the need arise;

Considering that such mutual assistance is only possible if the character and use of such blood-grouping reagents are subject to rules laid down jointly by the member countries and if the necessary import facilities and exemptions are granted,

Have agreed as follows:

Article 1

For the purposes of this Agreement, the expression "blood-grouping reagents" refers to reagents of human, animal and plant and other origin, used for blood-grouping and for the detection of blood incompatibilities.

Any Contracting Party may, by a declaration addressed to the Secretary General of the Council of Europe, when signing this Agreement or depositing its instrument of ratification or approval, or accession, limit the application of this Agreement to blood-grouping reagents of human origin. This declaration may be withdrawn at any time, by notification addressed to the Secretary General of the Council of Europe.

Article 2

The Contracting Parties undertake, provided that they have sufficient stocks for their own needs, to make blood-grouping reagents available to other Parties who are in urgent need of them and to charge only those costs of collection, processing and carriage of such substances and the cost (if any) of their purchase.

Article 3

Blood-grouping reagents shall be made available to the other Contracting Parties subject to the condition that no profit is made on them, that they shall be used solely for medical purposes and shall be delivered only to bodies designated by the governments concerned.

Article 4

The Contracting Parties shall certify that the provisions as laid down in the Protocol to this Agreement have been observed.

They shall also comply with any rules to which they have subscribed with regard to international standardisation in this field.

All consignments of blood-grouping reagents shall be accompanied by a certificate to the effect that they were prepared in accordance with the specifications in the Protocol. This certificate shall be based on the model to be found in the Annex to the Protocol.

The Protocol and its Annex constitute an administrative arrangement and may be amended or supplemented by the governments of the Parties to this Agreement.

Article 5

The Contracting Parties shall take all necessary measures to exempt from all import duties the blood-grouping reagents placed at their disposal by the other Parties.

They shall also take all necessary measures to provide for the speedy delivery of these substances, by the most direct route, to the consignees referred to in Article 3 of this Agreement.

Article 6

The Contracting Parties shall forward to one another, through the Secretary General of the Council of Europe, a list of the bodies empowered to issue certificates as provided in Article 4 of this Agreement.

They shall also forward a list of bodies empowered to distribute imported blood-grouping reagents. Wherever possible these bodies should be the same as those referred to in Article 6 of the European Agreement on the Exchange of Therapeutic Substances of Human Origin.

Article 7

The present Agreement shall be open to the signature of Members of the Council of Europe, who may become Parties to it either by:

a) signature without reservation in respect of ratification or approval, or

b) signature with reservation in respect of ratification or approval, followed by ratification or approval.

Instruments of ratification or approval shall be deposited with the Secretary General of the Council of Europe.

Article 8

The present Agreement shall enter into force one month after the date on which three Members of the Council shall, in accordance with Article 7, have signed the Agreement without reservation in respect of ratification or approval or shall have ratified or approved it.

In the case of any Member of the Council who shall subsequently sign the Agreement without reservation in respect of ratification or approval or who shall ratify or approve it, the Agreement shall enter into force one month after the date of such signature or the date of deposit of the instrument of ratification or approval.

Article 9

After the entry into force of this Agreement, the Committee of Ministers of the Council of Europe may invite any non-member State to accede to the present Agreement. Such accession shall take effect one month after the date of deposit of the instrument of accession with the Secretary General of the Council of Europe.

Article 10

The Secretary General of the Council of Europe shall notify Members of the Council and acceding States:

a) of the date of entry into force of this Agreement and of the names of any Members who have signed without reservation in respect of ratification or approval or who have ratified or approved it;
b) of the deposit of any instrument of accession in accordance with Article 9;
c) of any declaration or notification received in accordance with the provisions of Article 1, paragraph 2;
d) of any notification received in accordance with Article 11 and its effective date;
e) of any amendment of the Protocol and of its Annex under Article 4, paragraph 4.

Article 11

The present Agreement shall remain in force indefinitely.

Any Contracting Party may terminate its own application of the Agreement by giving one year's notice to that effect to the Secretary General of the Council of Europe.

In witness whereof the undersigned, duly authorised thereto by their respective Governments, have signed the present Agreement.

Done at Strasbourg, this 14th day of May 1962, in English and French, both texts being equally authoritative, in a single copy which shall remain deposited in the archives of the Council of Europe. The Secretary General shall transmit certified copies to each of the signatory and acceding Governments.

PROTOCOL TO THE EUROPEAN AGREEMENT
ON THE EXCHANGE OF BLOOD-GROUPING REAGENTS

GENERAL PROVISIONS

1. Specificity

A blood-grouping[1]) reagent must react with all blood samples tested which contain the antigen homologous to the antibody or other substance mentioned on the label.

When a reagent is used according to the technique recommended by the producer there must be no evidence of any of the following factors or phenomena:
(a) haemolytic properties;
(b) antibodies or other substances besides those mentioned on the label;
(c) bacterial products liable to cause false positive or false negative reactions;
(d) pseudo-agglutination through the formation of rouleaux;
(e) prozone phenomena.

2. Potency

Titre is measured by making successive two-fold dilutions of the reagent under study in an appropriate medium. To each dilution is added an equal volume of a susension of red corpuscles. The titre is the reciprocal of the figure representing the highest serum dilution in which a reaction occurs, the dilution being calculated without the inclusion of the volume of the corpuscular suspension in the total volume.

In the case of anti-A, anti-B and other reagents intended for use on slides, avidity is expressed by means of the time required for agglutination on a slide.

3. International Standards and International Units

International Standards have been established by the World Health Organization for anti-A and anti-B and incomplete anti-D blood-grouping reagents and are in process of being established for blood-grouping reagents of other specificities.

An International Standard Preparation contains, by definition, a certain number of International Units per mg or ml and this definition is independent of the titres observed against particular red corpuscle preparations.[2])

4. Stability and expiry date

Each reagent, when kept under the conditions of storage recommended by the manufacturer, should retain the requisite properties for at least one year.

The expiry date of a reagent in the liquid form as given on the label shall be not more than one year from the date of the last satisfactory potency test. The expiry date can be extended for further periods of one year by repetition of potency tests.

The expiry date of reagents in the dried form as given on the label shall be in accordance with evidence obtained from experiments on stability and shall be approved by the national control authorities.

5. Preservation

Blood-grouping reagents may be preserved in the liquid or dried state. Dried reagents shall be kept in an atmosphere of an inert gas or in vacuo, in the glass container in which they were dried and which shall be closed so as to exclude moisture. A dried reagent must not lose more than 0,5 % of its weight when tested by further drying over phosphorus pentoxide at a pressure not exceeding 0,02 mm of mercury for 24 hours.

Reagents shall be prepared with aseptic precautions and shall be free from bacterial contamination. In order

[1]) At the time of approving the present version of the Protocol and its Annexes, it was understood by the representatives of the Contracting Parties that when in the English text of the Agreement the expresions "blood incompatibilities" was mentioned, "blood grouping incompatibilities" was implied.
It was also agreed that the expression "blood-grouping" with a hyphen in the English text on the Agreement and of the Protocol should read as "blood grouping" without a hyphen.

[2]) The potency of blood-grouping reagents of most specificities is expressed as the agglutination titre observed in a dilution series, against a suspension of red cells. The titre indicates the dilution of reagent in the last mixture of the series which shows agglutination microscopically visible.
The potency of blood-grouping reagents for which International Standard Preparations exist (at present anti-A and anti-B and incomplete anti-D) can abe expressed in International Units (see Bull, Wld. Hlth. Org. 1954, 10, 937 – 1950, 3, 301) on the basis of the titration of the unknown reagent in comparison with the International Standard, or a national sub-standard.
The International Standard Preparations of blood-grouping sera are dispensed in ampoules containing dried human serum. When reconstituted to the volume of 1 ml, the anti-A and anti-B sera contain by definition 256 International Units per ml. They can be obtained free of charge, from the International Laboratory for Biological Standards of WHO, Statens Seruminstitut, Copenhagen.
The following table shows an example of a comparative titration of the International Standard anti-A Serum (S) and an 'unknown' anti-A reagent (U) against A_1 red corpuscles and A_2B red corpuscles.

	Serum S	Reagent U	Serum S	Reagent U
A_1 corpuscles	1 : 512	1 : 128	256	64
A_2B corpuscles	1 : 32	1 : 16	256	128
	titres (observed)	titres (observed)	Units (by definition)	Units (by comparison)

to prevent bacterial growth the competent national authority may decide that an antiseptic and/or antibiotic shall be added to the reagent (or to any solvent issued with dried reagents), provided that, in the presence of the added substance, the reagent still fulfils the requirements for specificity and potency.

Blood-grouping sera of human origin must contain at least 2,5 mg of protein nitrogen per ml of liquid or reconstituted serum.

Reagents whether in the liquid state or after reconstitution should be transparent and should not contain any sediment, gel or visible particles.

6. Coloration

Blood-grouping reagents for international exchanges should preferably not be artificially coloured at least until an international agreement is reached on a uniform system. Any added colouring matter must not interfere with the specific reaction.

7. Dispensing and volume

Blood-grouping reagents shall be dispensed in such a way and in such volumes that the reagent in one container is sufficient for the performance of tests with positive and negative control corpuscles in addition to the performance of tests with the unknown corpuscles. The volume in one container shall be such that the contents can if necessary be used for the performance of the appropriate tests for potency described in this Protocol.

8. Records and samples

Written records shall be kept by the producing laboratory of all steps in the production and control of blood-grouping reagents. Adequate samples of all reagents issued shall be retained by the laboratory until it can be reasonably assumed that the batch is no longer in use.

9. Classification of reagents

Reagents used for blood-grouping may contain substances of human, animal, vegetable (or mineral) origin, of which some constitute the active principle and others are adjuvants for enhancing the activity or maintaining the stability of the reagent.

For technical reasons these reagents have been divided into three categories according to the origin of their active principle. This does not mean that reagents of human origin contain exclusively substances of human origin or that animal or vegetable reagents cannot contain substances of human origin.

10. Labels, leaflets and certificates

A label printed in English and French, in black on white paper, shall be affixed to each final container and shall contain the following information:

1. Name and address of producer;
2. Name of the reagent as it appears in the heading of the relevant specification;
3. Name and amount of antiseptic and/or antibiotic, if present, or indication of absence;
4. The volume or, where the reagent is dried, the volume and composition of the fluid needed for reconstitution;
5. Expiry data;
6. Batch number.

Moreover, this label or the label of the carton enclosing several final containers, or the leaflet accompanying the containers, shall contain the following information:

1. Full name and address of producer;
2. Name of the reagent as it appears in the heading of the relevant specification;
3. The volume, or, where the reagent is dried, the volume and composition of the fluid needed for reconstitution;
4. Date of last potency test;
5. Expiry date (if any);
6. Batch number;
7. Adequate description of the method of use recommended by the producer;
8. Conditions of storage of unopened ampoules and precautions to the taken after opening;
9. Exact composition, including antiseptic and/or antibiotic if any;
10. Statement whether the product contains or does not contain material of human origin.

Each consignment shall be accompanied by a certificate as provided in Article 4 of the Agreement and the Annex to the present Protocol. Examles of labels and leaflets are attached to the resent Protocol.

SPECIFIC PROVISIONS

A. BLOOD-GROUPING SERA OF HUMAN ORIGIN

(a) SERA OF HUMAN ORIGIN FOR ABO GROUPING

(i) Anti-A blood-grouping serum (human)

Anti-A serum is derived from the blood of selected group B persons, who may or may not have been immunized by group A red corpuscles or group A specific substance. Anti-A serum agglutinates human red corpuscles containing A antigen, i.e. those of blood groups A and AB, including sub-groups, A_1, A_2. A_1B and A_2B, and does not agglutinate human red corpuscles which do not contain A antigen, i.e. those of blood groups 0 and B.

Potency

Titration

An anti-A serum shall be titrated separately against suspensions of A_1, A_2 and A_2B corpuscles, in parallel with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or an equivalent reference preparation. The potency of the serum shall in each case be not less than 64 International Units per ml.

Determination of avidity

When anti-A serum is mixed on a slide with an equal volume of a suspension of A_1, A_2 and A_2B cells with a volume fraction of 0,05 to 0,1, agglutination of each suspension should first appear in not more than twice the time taken when the same test is performed with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or with a reference standard of equivalent avidity.

(ii) Anti-B blood-grouping serum (human)

Anti-B serum is derived from the blood of selected group A persons, who may or may not have been immunized by group B red corpuscles or group B specific substance. Anti-B serum agglutinates human red corpuscles containing B antigen, i.e. those of blood groups B and AB, and does not agglutinate human red corpuscles which do not contain B antigen, i.e. those of blood groups 0 and A.

Potency

Titration

An anti-B serum shall be titrated against a suspension of group B corpuscles in parallel with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or an equivalent reference preparation. The potency of the serum shall be not less than 64 International Units per ml.

Determination of avidity

When anti-B serum is mixed on a slide with an equal volume of a suspension of B cells with a volume fraction of 0,05 to 0,1, agglutination should first appear in not more than twice the time taken when the same test is performed with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or with reference standard of equivalent avidity.

(iii) Anti-A + Anti-B (group) blood-grouping serum (human)

Anti-A + anti-B (group 0) serum is derived from the blood of selected group 0 persons who may or may not have been immunized by group A and group B red corpuscles or group A and group B specific substances. Anti-A + anti-B (group 0) serum agglutinates human red corpuscles containing A or B agglutionogens or both, i.e. those of group A including subgroups A_1 and A_2, group B and group AB including subgroups A_1B and A_2B, and does not agglutinate human red corpuscles which do not contain A or B agglutinogens, i.e. those of group 0. It agglutinates human red corpuscles containing the A_x (A_y or A_o) antigen (which are not, in general, agglutinated by anti-A serum derived from group B donors).

Potency

Titration

An anti-A + anti-B (group 0) serum shall be titrated separately against suspensions of A_1, and A_2 corpuscles in parallel with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or an equivalent standard preparation. It shall also be titrated against a suspension of group B corpuscles in parallel with the reconstituted but undiluted International Standard Preparation of anti-B blood grouping serum or an equivalent standard preparation.

The potency of the serum shall in every case be not less than 64 International Units per ml.

Anti-A + anti-B (group 0) blood-grouping serum used undiluted shall also give readily detectable agglutination of group A_x (A_y or A_o) corpuscles.

Determination of avidity

When anti-A + anti-B (group 0) serum is mixed on a slide with equal volumes of suspensions of A_1 and A_2 cells with a volume fraction of 0,05 to 0,1, agglutination shall first appear in not more than twice the time taken when the same tests are performed with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or with a reference standard of equivalent avidity. When anti-A + anti-B (group 0) serum is mixed on a slide with an equal volume of a suspension of B cells with a volume fraction of 0,05 to 0,1, agglutination shall first appear in not more than twice the time taken when the same est is performed with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or a reference preparation of equivalent avidity. When anti-A + anti-B (group 0) serum is mixed on a slide with an equal volume of a suspension of A_x (A_y or A_o) cells with a volume fraction of 0,05 to 0,1, agglutination shall first appear in not more than five minutes at a temperature between 18 and 25 °C.

(b) SERA OF HUMAN ORIGIN FOR Rh GROUPING

Anti-Rh blood-grouping sera, whatever their specificity, may be of either of two varieties differing in the conditions under which agglutination of homologous corpuscles is obtained. Certain sera commonly known as 'complete' agglutinate corpuscles suspended in saline. With others, commonly known as 'incomplete', agglutination can only be obtained in the presence of certain colloids such as bovine albumin or by means of other special techniques. The sera should by used under the conditions specified by the laboratory preparing them.

Some 'incomplete' sera will also agglutinate homologous red corpuscles suspended in their own serum or plasma on slides.

The following requirements of potency for Rh

grouping sera may need to be revised when International Standard Preparations become available.

(i) Anti-D (anti-Rh_o) blood-grouping serum (human)

Anti-D serum is derived from the blood of one or more persons immunized by the D antigen of the Rh system. It reacts with human red corpuscles containing the D antigen, but not with human red corpuscles which do not contain the D antigen.

Potency

Titration

'Complete' anti-D sera shall have a titre of not less than 32 against CcDee cells in a solution containing 9 grams sodium chloride per litre.

An 'incomplete' anti-D serum shall be titrated against CcDee corpuscles in parallel with the reconstituted but undiluted International Standard Preparation of Incomplete Anti-D (anti-Rho) or an equivalent reference preparation. It shall have a potency of not less than 32 International Units. Besides reacting with all red corpuscles containing the D antigen, the serum should, as far as possible, react with corpuscles containing the D^u antigen.

Determinati on of avidity

Anti-D sera intended for use in the slide test of Diamond and Abelson should, when mixed on a slide with an equal volume of a 40 to 50 % suspension of CcDee corpuscles at aproximately 40 °C, show visible agglutination within 30 seconds, and agglutination should be complete within 120 seconds.

(ii) Anti-C (anti Rh) blod-grouping serum (human)

Anti-C serum is derived from the blood of one or more persons immunized by the C agglutinogen of the Rh system. It agglutinates suspensions of human red corpuscles containing the C antigen, but not with human red corpuscles which do not contain the C antigen. In this connection the C antigen is regarded as including the C^w antigen.

Most diagnostic anti-C sera contain 'complete' anti-C together with 'incomplete' anti-D. These sera are therefore specific for the C antigen only when the cells under test are suspended in a solution containing 9 grams sodium chloride per litre.

Potency

Titration

Anti-C sera ('complete' or 'incomplete') should have a titre of not less than 8 against Ccddee corpuscles.

Determination of avidity

Anti-C sera intended for use in the slide test of Diamond and Abelson (and which must not contain any form of anti-D) should, when mixed on a slide with an equal volume of a suspension of Ccddee cells with a volume fraction of 0,4 to 0,5, at approximately 40 °C, show visible agglutination within 30 seconds, and agglutination should be complete within 120 seconds.

(iii) Anti-E (anti-Rh*) blood-grouping serum (human)

Anti-E serum is derived from the blood of one or more persons immunized by the E antigen of the Rh system. It reacts with human red corpuscles containing the E antigen.

Potency

Titration

Anti-E sera ('complete' or 'incomplete') should have a titre of not less than 8 against ccddEe corpuscles.

Determination of avidity

Anti-E sera intended for use in the slide test of Diamond and Abelson (and which must contain any form of anti-D) should, when mixed on a slide with an equal volume of a suspension of ccddEe cells with a volume fraction of 0,4 to 0,5, at approximately 40 °C, show visible agglutination within 30 seconds, and agglutination should be complete within 120 seconds.

(iv) Anti-D + C (anti/Rh_oRh) blood-grouping serum (human)

Anti-D + E (anti-Rh_oRh*) blood-grouping serum (human)

Sera of specificity anti-D + C and of specificity anti-D + E may be obtained directly from the blood of immunized individuals or may be prepared by mixing anti-D with anti-C or anti-E serum. In a given serum both anti/bodies must be simultaneously active under the conditions of reaction specified by the producer. Each serum must react with all types of red corpuscles which would react with either of the component antibodies, and must fail to react with red corpuscles which contain neither the C nor D antigen in the case of anti-D + C and neither D nor E antigen in the case of anti-D + E. The titres should not be less than those specified for the component antibodies, but in the case of anti-D + C (which is a frequent combination in the serum of immunized persons) it is desirable that the anti-C titre should be not less than 32 and in the case of anti-D + E it is desirable that the anti-E titre should be not less than 8. Where a serum is intended for use in the slide test of Diamond and Abelson, the times of agglutination for all reacting types of red corpuscles should be not less than those specified for the component antibodies.

B. REAGENTS OF NON-HUMAN ORIGIN

(a) SERA OF ANIMAL ORIGIN

(i) Anti-A blood-grouping serum (animal)

Anti-A serum is derived from the blood of animals which may or may not have been immunized by group A red corpuscles or group A specific substances. Anti-A serum agglutinates human red corpuscles containing A antigen, i.e. those of blood groups A and AB, including sub-groups A_1, A_2, A_1B and A_2B, and does not agglutinate human red corpuscles which do not contain A antigen, i.e. those of blood groups 0 and B.

Potency

Titration

An anti-A serum shall be titrated separately against suspensions of A_1, A_2 and A_2B red corpuscles, in parallel with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or an equivalent reference preparation (1). The potency of the serum shall in each case be not less than 64 International Units per ml.

Determination of avidity

When anti-A serum is mixed on a slide with an equal vlume of a suspension of A_1, A_2 and A_2B cells with a volume fraction of 0,05 to 0,1, agglutination of each suspension shall in each case first appear in not more than twice the time taken when the same test is performed with the reconstituted but undiluted International Standard Preparation of anti-A blood-rouping serum or with a reference standard of equivalent avidity.

(ii) Anti-B blood-grouping serum (animal)

Anti-B serum is derived from the blood of animals which may or may not have been immunized by group B red corpuscles or group B specific substances. Anti-B serum agglutinates human red corpuscles containing B antigen i.e. those of blood groups B and AB, and does not agglutinate human red corpuscles which do not contain B antigen, i.e. those of blood groups 0 and A.

Potency

Titration

An anti-B serum shall be titrated against a suspension of group B corpuscles in parallel with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or an equivalent reference preparation[1]). The potency of the serum shall be not less than 64 International Units per ml.

Determination of avidity

When anti-B serum is mixed on a slide with an equal volume of a suspension of B cells with a volume fraction of 0,05 to 0,1, agglutination shall first appear in not more than twice the time taken when the same test in performed with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or with a reference standard of equivalent avidity.

(iii) Anti-human-globulin serum (animal)[2])

Anti-human globulin serum for use in blood group serology must contain agglutinating antibodies against IgG globulin and agglutinating antibodies against complement factors. It is derived from the blood of animals immunized by the injection of human serum protein. It must agglutinate all human red corpuscles coated with human IgG and/or complement factors. Under the conditions specified by the manufacturers it does not agglutinate uncoated human red corpuscles, to whatever group they may belong.

Specificity

The specificity of an anti-human globulin serum for use in blood group serology must be tested with human red corpuscles coated with a variety of antibodies i.e. red corpuscles sensitized with human incomplete antibodies anti-D, anti-K and anti-Fya, red corpuscles sensitized with complement-binding incomplete antibodies anti-Lea in the presence of fresh human serum, and red corpuscles sensitized with socalled 'incomplete cold antibodies' and with tanned red corpuscles sensitized with human IgG and, finally, with 10 different samples of non-coated human red corpuscles with and without A and B antigens.

Potency

Titration

An anti-human globulin serum, as supplied, or at the dilution recommended on the label, shall strongly agglutinate human red corpuscles coated with a human incomplete anti-D serum, having a titre of 4 (or less) against D-positive corpuscles, when the titration is performed by the albumin replacement method. At the same dilution it shall agglutinate K-positive human corpuscles sensitized with selected weak anti-K antibodies and Fy^a positive red corpuscles sensitized with selected weak anti-Fy^a antibodies.

It shall also, at the same or a different dilution, as

[1]) The International Standard Preparation is of human origin: an equivalent reference preparation, if used, may be of human or non-human origin.

[2]) Coombs, R.R.A., Mourant, A.E. and Race, R.R. (1945), Lancet, iii5.
Coombs, R.R.A., Mourant, A.E. and Race, R.R. (1945), Brit. J.exp. Path, 26, 255.
At the same dilution it shall agglutinate K-positive human red corpuscles sensitized with selected weak anti-K antibodies and Fy^a positive red corpuscles sensitized with selected weak anti-Fy^a antibodies.
It shall also, at the same or a different dilution, as specified on the label, agglutinate human red corpuscles sensitized with weak complement-binding incomplete anti-Le^a antibodies in the presence of fresh serum.
For clinical use it is desirable that the coating of all the types of incomplete antibodies above shall be detectable with a single dilution of the anti-human globulin serum.

specified on the label, agglutinate human red corpuscles sensitized with weak complement-binding incomplete anti Le^a antibodies in the presence of fresh serum.

Foe clinical use it is desirable that the coating of all the types of incomplete antibodies above shall be detectable witha single dilution of the ant-human globulin serum.

(b) BLOOD-GROUPING REAGENTS OF VEGETABLE ORIGIN

(i) Anti-A blood-grouping reagent (vegetable)

Anti-A reagent is prepared by extraction from the seeds or other parts of a suitable plant, followed, if necessary, by purification. Anti-A reagent agglutinates human red corpuscles containing A antigens, i.e. those of blood groups A and AB, including sub-groups A_1, A_2, A_1B and A_2B and does not agglutinate human red corpuscles which do not contain A antigens, i.e. those of blood groups 0 and B.

Potency

Titration

An anti-A reagent shall be titrated separately against suspensions of A_1, A_2 and A_2B corpuscles, in parallel with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or an equivalent reference preparation.[1])

The potency of the reagent shall in each case be not less than 64 International Units per ml.

Determination of avidity

When anti-A reagent is mixed on a slide with an equal volume of a suspension of A_1, A_2 and A_2B cells with a volume fraction of 0,05 to 0,1, agglutination of each suspension shall first appear in not more than twice the time taken when the same test is performed with the reconstituted but undiluted International Standard Preparation of anti-A blood-grouping serum or with a reference standard of equivalent avidity.

(ii) Anti-B blood-grouping reagent (vegetable)

Anti-B reagent is prepared by extraction from the appropriate parts of a suitable plant, followed, if necessary, by purification. Anti-B reagent agglutinates human red corpuscles containing B antigens, i.e. those of blood groups B and AB, and does not agglutinate human red corpuscles which do not contain B antigen, i.e. those of blood groups 0 and A.

Potency

Titration

An anti-B reagent shall be titrated against a suspension of group B corpuscles in parallel with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or an equivalent reference preparation.[1]) The potency of the reagent shall not be less than 64 International Units per ml.

Determination of avidity

When anti-B reagent is mixed on a slide with an equal volume of a suspension of B cells with a volume fraction of 0,05 to 0,1, agglutination shall first appear in not more than twice the time taken when the same test is performed with the reconstituted but undiluted International Standard Preparation of anti-B blood-grouping serum or with a reference standard of equivalent avidity.

[1]) The International Standard Preparation is of human origin; an equivalent reference preparation, if used, may be of human or non-human origin.

EXAMPLES D´ÉTIQUETE

EXAMPLES OF LABEL

CONSEIL DE L´EUROPE

COUNCIL OF EUROPE

Accord européen relatif á l´échange des réacifs pour la détermination des groupes sanduins

European Agreement on the exchange of blood – grouping reagents

a) sérum liquide	**a) fluid serum**
1. Laboratoire X, Amsterdam 2. Sérum anti-A (humain) 3. N_1Na 0,1 % 4. 5 ml 5. 7 septembre 1965 6. N 1 2 3 4	1. ...Laboratory, Amsterdam 2. Anti-A serum (human) 3. Sodium azide 0,1 % 4. 5 ml 5. 7 september 1965 6. No 1 2 3 4
b) sérum desséché	**b) dried serum**
1. Laboratoir X, Amsterdam 2. Sérum anti – B (animal) (a) Mersalate 0,1 % (b) Reconstituer avec 5 ml d´eau distillée (c) 31 décembre1968 (d) N 4 3 2 1	1. ...Laboratry, Amsterdam 2. Anti – B serum (animal) 3. Mersalate 0,1 % 4. To be reconstitued with 5 ml distilled water 5. 31 December1968 6. No 4 3 2 1

EXAMPLE OF LEAFLET

COUNCIL OF EUROPE

European Agreement on the exchange of blood – grouping reagents

1. Central Blood Transfusion Laboratory, 1 Main Street, Metropolis, Westland
2. Anti-E ("anti-Rh") serum (human)
3. 10 ml
4. Date of the last co-test: 10th May 1961
5. Expiry Date 30th May 1962
6. No. 5432
7. The red blood cells to be tested are washed one or more time with NaCl solution of 9 g/l. An erythrocyte suspension with a volume fraction of 2 approximately 0,03 is prepared by mixing one volume or drop of packed red cells with 10 volumes or drops of isotonic NaCl-solution. With practice the strength of a suspension can be judged adequately by inspection.

A small drop of serum is delivered into a precipitin tube (6 mm x 30 mm) from a Pasteur pipette, and a similar drop of red corpuscle suspension is added. (With practice considerable economy can be achieved by delivering the serum and cell suspension from pipettes marked at the volume of 10 ml.) The contents of the tube are mixed and incubated at 37 C for two hours The contents of the tube are then cautiously transferrred to a microscope slide and gently spread upon it. Unless agglutination is unmistakeable to the nuaided eye the slide is examined for the presence and degree of agglutination under the microscope.

8. Store at - 20 °C or bellow If to be used after day of opening, add 0,1 of a solution containing 100 gram sodium azide per litre.
9. Human anti-E (anti-Rh) serum: 5 ml solution containing 300 gram bovine albumine per litre: 5 ml.
10. The product contains material of human origin.

ANNEXE AU PROTOCOLE

ANNEX TO THE PROTOCOL

COSEIL DE L´EUROPE

COUNCIL OF EUROPE

Aaccord européen relatif á l´échange des réactifs pour la détermination de groupes sanguins

European Agreement on the exchange of blood-grouping reagents

CERTIFICAT

(Article 4)

A ne pas détacher de l´envoi
Not to be separated from the shipment

..... 19.....
(lieu) (date)
(place)

Nombre de colis Le sousigné déclare que l´envoi spécificé en marge
Number of packages The undersigned certifies that the shipment certified in the margin
. . . . . .
. . . . . .
. . . . . .

Désignation préparé sous la responsbilité de
Marked prepared under the responsibility of
. . . . . .
. . . . . .

No des lots organisme visé á l´article 6 de l´accord rst conforme aux spécifications du
Batch No protocole a l´accord et qu´il peut etre délivré immédiatement au destinataire
. . . . . (nom et lieu) . . . . . .
. . . . . .
. . . . . .
. . . . . .
one of the bodies reffered to in Article 6 of the Agreement is in conformity with the specifications of the Protocol and can be delivered immidiately to the consignee (name and place)

(cachet) (signature) (titre)
(stamp) (signature) (title)

CERTIFICATE

ADDITIONAL PROTOCOL TO THE EUROPEAN AGREEMENT ON THE EXCHANGE OF BLOOD-GROUPING REAGENTS

The member States of the Council of Europe, Contracting Parties to the European Agreement of 14 May 1962 on the exchange of blood-grouping reagents (hereinafter called "the Agreement"),

Having regard to the provisions of Article 5, paragraph 1, of the Agreement, according to which "The Contracting Parties shall take all necessary measures to exempt from all import duties the blood grouping reagents placed at their disposal by the other Parties";

Considering that so far as the member States of the European Economic Community are concerned, the undertaking to grant this exemption falls within the competence of the Community, which possesses the necessary powers in this respect by virtue of the treaty which instituted it;

Considering therefore that for the purpose of the implementation of Article 5, paragraph 1, of the Agreement, it is necessary for the European Economic Community to be able to become a Contracting Party to the Agreement,

Have agreed as follows:

Article 1

The European Economic Community may become a Contracting Party to the Agreement by signing it. In respect of the Community, the Agreement shall enter into force on the first day of the month following such signature.

Article 2

1 This Additional Protocol shall be open for acceptance by the Contracting Parties to the Agreement. It shall enter into force on the first day of the month following the date on which the last of the Contracting Parties has deposited its instrument of acceptance with the Secretary General of the Council of Europe.

2 However, this Additional Protocol shall enter into force on the expiration of a period of two years from the date on which it has been opened for acceptance, unless one of the Contracting Parties has notified an objection to the entry into force. If such an objection has been notified, paragraph 1 of this article shall apply.

Article 3

From the date of its entry into force, this Additional Protocol shall form an integral part of the Agreement. From that date, no State may become a Contracting Party to the Agreement without at the same time becoming a Contracting Party to the Additional Protocol.

Article 4

The Secretary General of the Council of Europe shall notify the member States of the Council of Europe, any State having acceded to the Agreement and the European Economic Community of any acceptance or objection made under Article 2 and of the date of entry into force of this Additional Protocol in accordance with Article 2.

The Secretary General shall also notify the European Economic Community of any act, notification or communication relating to the Agreement.

Done at Strasbourg, the 29th day of September 1982, in English and in French, and opened for acceptance the 1st day of January 1983. Both texts are equally authentic and shall be deposited in a single copy in the archives of the Council of Europe. The Secretary General of the Council of Europe shall transmit certified copies to each member State of the Council of Europe, to any State invited to accede to the Agreement and to the European Economic Community.