

PROGRESS IN



**IMMUNOBIOLOGICAL
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1

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for Microbiological Standardization, Bern 1962

Edited by

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International Association of Microbiological Societies

Permanent Section of Microbiological Standardization

8th Congress: Bern 1962

Proceedings of the 8th International Congress for Microbiological Standardization, held at the Kursaal of Bern, June 18–21, 1962. Edited by: R. H. REGAMEY, Institut d'Hygiène, Genève; H. HENNESSEN, Behringwerke AG, Marburg a.L.; D. IKIĆ, Serovakcinolni Zavod, Zagreb; J. UNGAR, Biological Department, Glaxo Laboratories Ltd., Greenford (Middx)

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Introduction

Why this new series of '*Progress in Immunobiological Standardization*'?

Within the framework of the '*International Association of Microbiological Societies*' those who are concerned on a day to day basis with the problems of control of sera, vaccines and other immunobiological products, whether they be State controllers, manufacturers or independent research workers, have formed the '*Permanent Section of Microbiological Standardization*'. One of the aims of this Section is to promote the creation and introduction of techniques of standardization and to support the efforts made by the World Health Organisation in the study, introduction and application of the International Biological Standards and International Biological Reference Preparations.

To this end the '*Permanent Section of Microbiological Standardization*' has organised two series of meetings. Some of these meetings are of a general nature and bring together members of the Section as well as those who are interested in the particular day's topics. The reports of these conferences have been published: Lyon 1955, Rome 1956, Opatijà 1957, Brussels 1958, Jerusalem 1959, Wiesbaden 1960, London 1961. These publications however lack a certain uniformity and it is hoped to overcome this and maintain uniformity in the future with the publication of '*Progress of Immunobiological Standardization*'. As there is no question of re-editing the works which have already appeared, the '*Progress*' will contain in its first volume the reports of the Eighth International meeting of Biological Standardization which took place in Berne in 1962. The topics covered in previous meetings are reported in the present volume page X.

In addition to the *meetings* where several topics are discussed, the '*Permanent Section of Microbiological Standardization*' organises *Round Table discussions*, which are devoted to the study of a single subject. The proceedings of these symposia have been duplicated or printed and distributed among the participants.

1st symposium: 65th anniversary of the Institutes of Immunology of Zagreb. Opatijà 1959 (printed)

2nd symposium: Problems of the immunobiological Standardization Opatijà 1960 (printed)

3rd symposium: Pertussis immunization, Praha 1962

4th symposium: Standardization of the vaccine, Lyon 1962 (printed)

5th symposium: The characterization and uses of human diploid cell strains, Opatijà 1963 (to be printed)

6th symposium: Standardization of the methods for the control of sterility, London 1963

It is desirable that the entire works concerning standardization should be collected in one series of publications. The '*Permanent Section of Microbiological Standardization*' is endeavouring to offer those interested in the problems of biological Standardization a source of information which is easily accessible and is at the same time a useful reference book.

The Editorial Committee of the
Permanent Section of Microbiological
Standardization

Introduction

Pourquoi cette nouvelle série de « *Progress in Immunobiological Standardization* »?

Au sein de l'« *International Association of Microbiological Societies* », ceux qui se trouvent aux prises journalières avec les problèmes du contrôle des sérums, vaccins et autres produits immunobiologiques, qu'ils soient contrôleurs d'états, fabricants ou chercheurs indépendants, se sont réunis et forment la « *Permanent Section of Microbiological Standardization* ». L'un des buts de cette Section est de promouvoir la création et la mise au point de techniques de standardisation et d'appuyer les efforts consentis par l'Organisation Mondiale de la Santé dans l'étude, l'introduction et l'application des étalons biologiques internationaux et des préparations biologiques internationales de référence.

La « *Permanent Section of Microbiological Standardization* » organise dans ce but deux séries de rencontres. Les unes ont un caractère général et réunissent l'ensemble des membres de la Section ainsi que tous ceux qu'intéressent les thèmes portés à l'ordre du jour. Les comptes-rendus de ces réunions ont fait l'objet de publications: Lyon 1955, Rome 1956, Opatijà 1957, Bruxelles 1958, Jérusalem 1959, Wiesbaden 1960, London 1961. Il manquait à ces publications un certain caractère d'unité, défaut qui sera dès maintenant éliminé par la création des « *Progress in Immunobiological Standardization* ». Comme il ne saurait être question de rééditer les œuvres déjà parues, la collection des « *Progress* » débute dans son tome 1 avec les comptes-rendus de la 8^e Rencontre Internationale de Standardisation biologique, tenue à Berne 1962. Les thèmes traités lors des rencontres précédentes sont rapportés dans le présent volume, page X.

Outre les *meetings* où plusieurs thèmes sont débattus, la « *Permanent Section of Microbiological Standardization* » organise des *Tables rondes*, qui sont consacrées à l'étude d'un thème unique. Les comptes-rendus de ces symposiums ont été soit multicotiés, soit imprimés.

1^{er} symposium: 65th anniversary of the Institutes of Immunology of Zagreb. Opatijà 1959 (printed)

2^e symposium: Problems of the immunobiological Standardization. Opatijà 1960 (printed)

3^e symposium: Pertussis immunization. Praha 1962

4^e symposium: Standardization of the vaccine. Lyon 1962 (printed)

5^e symposium: The characterization and uses of human diploid cell strains. Opatijà 1963 (to be printed)

6^e symposium: Standardization of the methods for the control of sterility. London 1963

Il est souhaitable que l'ensemble des travaux touchant à la standardisation puissent être réunis dans une même série de publications. La « *Permanent Section of Microbiological Standardization* » va tenter de valoriser ses efforts au maximum en offrant à ceux qu'intéressent les problèmes de standardisation biologique une source de renseignements aisément accessibles et un précieux instrument de travail.

Le comité de rédaction de la
Section Permanente de
Standardisation Microbiologique

Topics Treated in the Meetings 1-7 (1955-1961) Sujets traités dans les rencontres 1-7 (1955-1961)

I

Première rencontre européenne de standardisation biologique

Lyon 1955 (22-25 juin) (Documents multicopiés)

Diphtheria Toxoid. *Holt, L. B.* (London): Preliminary order of the day for the discussions on the diphtheria anatoxin. - *Barr, M.* (Beckenham): Diphtheria toxoid. - *d'Antona, D. et Piazzzi, S.* (Siena): Effets de la variation quantitative et qualitative des stimulations antigéniques primaires et secondaires. Mécanisme d'action des adjuvants de l'immunité. - *Scheibel, I. et Bojlen, K.* (Copenhagen): Results of a field examination in Denmark on the duration of immunity after diphtheria vaccination and of the laboratory testing of the vaccine. - *Ikit, D.* (Zagreb): Standardization of diphtheria prophylactics. - *Vygodtchikov, G. V.* (Moscow): Les recherches sur la standardisation et le contrôle de l'anatoxine diphtérique dans les laboratoires soviétiques. - Discussion: *Barr, M.* (Beckenham) - *Fisek, N. H.* (Ankara) - *Holt, L. B.* (London) - *Maaloe, O.* (WHO Geneva) - *Meisel, H.* (Warsaw) - *Nicol, L.* (Paris) - *Perry, W. L. M.* (London).

Tetanus Toxoid. *Fisek, N. H.* (Ankara): Tetanus toxoid. - *Petrović, D.* (Belgrad): La production de la toxine de Cl. tetani. - *Petrović, D.* (Belgrad): La détermination de la valeur antigène de l'anatoxine tétanique précipitée par l'alun ainsi que de la même anatoxine associée au vaccin typhoparatyphique A et B. - *Djouricbić, M. et Katit, R.* (Belgrad): Neutralisation de l'anatoxine tétanique et de l'antitoxine. Importance pratique. - *Fisek, N. H.* (Ankara): The application of the neutralization inhibition phenomenon to the quantitative determination of toxoids. - *Ikit, D.* (Zagreb): Standardization of tetanus prophylactics. - *Vygodtchikov, G. V.* (Moscow): Les recherches sur la standardisation et le contrôle de l'anatoxine tétanique dans les laboratoires soviétiques - *Grasset, E.* (Geneva): Standardization of the anatoxine tétanique. - Discussion: *d'Antona, D.* (Siena) - *Djouricbić, M.* (Belgrad) - *Fisek, N. H.* (Ankara) - *Grabar, P.* (Paris) - *Holt, L. B.* (London) - *Ikit, D.* (Zagreb) - *Lafontaine, A.* (Bruxelles) - *Lourie, E. M.* (WHO, Geneva) - *Maaloe, O.* (WHO, Geneva) - *Perry, W. L. M.* (London) - *Regamey, R. H.* (Bern) - *Scheibel, I.* (Copenhagen) - *Vygodtchikov, G. V.* (Moscow).

Tuberculin in Human Medicine. *Sansonetti, R.* (Bern): Standardisation et contrôle des tuberculines en médecine humaine. - *Fisek, N. H.* (Ankara): Standardization of tuberculin. - *Svenkerud, R.* (Oslo): Standardization of tuberculin. The intracutaneous method on Guinea pigs. - *Desbordes, J. et al.* (Paris): Etude électrophorétique et clinique de la tuberculine. - *Desbordes, J.* (Paris): Contribution au contrôle des préparations tuberculiniques. - *Ribeiro, J. M.* (Lisbon): Tuberculines purifiées et leurs fractions protéiniques. - *Despières, G. et Caigzinger* (Lyon): Etude clinique de la fragmentation électrophorétique de la tuberculine. - Discussion: *Bretay, J.* (Paris).

Tuberculin in Veterinary Medicine. *Plum, N.* (Copenhagen): Concerning tuberculin in veterinary medicine. - *Mérieux, C.* (Lyon): Sur la stabilité de la tuberculine préparée sur milieu synthétique. - *McGirr, W.* (Weybridge): Tuberculinisation des bovins. Emploi des tuberculines P.P.D. de Weybridge. - *Panisset, M.* (Montreal): La standardisation des tuberculines au Canada. - *Finzgi, G.* (Milan): La standardisation et le contrôle des tuberculines en médecine vétérinaire. - Discussion: *Fluckiger, G.* (Bern).

Poliomyelitis Vaccine. Abstract from "Hessischer Staatsanzeiger". - *Haas, R.* (Marburg a/L): Remarques à propos du contrôle et de la standardisation des vaccins poliomyélitiques. - *Hammon, W. McD.* (Pittsburgh, Pa): Sur les problèmes que soulève la standardisation dans la préparation du vaccin contre la poliomyélite en grande quantité aux Etats-Unis. - *Lépine, J.* (Paris): Discussion à propos du rapport du Dr Hammon. - *Von Magnus, H.* (Copenhagen): On the production of polio vaccine in Denmark. - *Neumüller, G.* (Stockholm): Vaccine against poliomyelitis in Sweden. - *Auerswald, W.* (Vienna): Poliomyelitisvaccine. - *Oddo, F. G.* (Palermo): Polio-vaccine. - Discussion: *Grasset, E.* (Geneva).

Gamma Globulin. *Ardry, R.* (Clamart, Seine): The Standardization and the control of gammaglobulin. - *Zahrzewski, K.* (Warsaw): Standardization of gammaglobulins. - *Hammon, W. McD.* (Pittsburgh, Pa): The use of gammaglobulin in poliomyelitis. - *Eibl, H.* (Vienna): Gammaglobulin. - *Manpin, B.* (Clamart, Seine): Considérations sur la posologie des gammaglobulines. Observations sur la prévention de la rougeole en milieu militaire. - *Mechalova, A.* (Moscow): Standardisation et contrôle des globulines gamma en Union Soviétique. - Discussions: *Ardry, R.* (Clamart, Seine) - *Entelme, J.* (Lyon) - *Grabar, P.* (Paris) - *Lewin, J.* (Paris) - *Pigouy, L.* (Alfort).

Recommendations.

II

Atti del secondo congresso internazionale di standardizzazione immunomicrobiologica

Roma 1956 (10-14 settembre) (Ed. Technica grafica, Via Gallia 150, Roma 1957)

Lactobacilli and Lactic Ferments. *Mattick, A. T. R. and Mabbitt, L. A.* (Shinfield): Enumeration and classification of lactobacilli. - *Negri, R. e von Lorch, L.* (Roma): Caratteristiche delle preparazioni farmaceutiche contenenti lattobacilli e loro controllo. - *Mattewuzzi, A. e Nobili, F.* (Bologna): Sopravvivenza dei lattobacilli alla liofilizzazione. - *Rghini, A., Malgeri, G. e Vidali, P.* (Milano): Prodotto ottenuto mediante liofilizzazione, contenente microorganismi resi resistenti a vari antibiotici e complesso B.

Pertussis Vaccine. *Ungar, J.* (Greenford): Assay of antigenicity of pertussis vaccines. - *Guerault, A.* (Montreal): H. pertussis: vaccins bactériens et antigènes purifiés. - *Pontecorvo, M. e Soprano, D.* (Napoli): Procedimenti di preparazione e conservazione del vaccino antipertossico. - *Kasuga, T.* (Tokyo): Relations between antigenic components and protective potency of H. pertussis. - *Jod I. and Crizmat, L.* (Budapest): Standardization and control of plain and combined pertussis vaccines in Hungary. - *Evans,*

D. G. (London): Laboratory tests in the study of pertussis immunity. - *Clévet, J. et Zourbas, J. (Razac s. l'Isle, Dordogne):* Etude clinique, immunologique et épidémiologique d'un vaccin anticoquelucheux, antidiphthérique et antitétanique mixte adsorbé. - *Martin du Pan, R. (Genève) et Zourbas, J. (Paris):* Contribution à l'étude de la vaccination anticoquelucheuse. I. II.

Polio Vaccine. *Workman, W. G. (Bethesda, Md.):* Standardization and control of poliomyelitis vaccine. - *Lépine, P. (Paris):* Etude critique des normes minimums (minimum requirements) américaines du vaccin antipoliomyélique inactif. - *Gorwe, E. G. (Indianapolis, Ind.):* Safety testing of poliomyelitis vaccine by tissue culture technique. - *Gard S. (Stockholm):* Aspects on production and control of formalin-treated poliovirus vaccines.

Smallpox Vaccine. *McClan, D. (Elstree):* The preparation, standardization and use of a purified stable dried smallpox vaccine. - *Westen, T. (Uppsala):* The production of smallpox vaccine in tissue culture of bovine embryonic skin. - *Kempe, C. H. (Rome):* Egg potency tests of dried smallpox vaccines of chick embryo origin. - *Metcalova, A. N. (Moscow):* Standardizatii i kontrol' ospennoi baktisiny v Sovetskom Soiuze. - *Baltazard, M., Srydian, B. et Chamsa, M. (Téhéran):* Préparation, standardisation et contrôle du vaccin antivariolique desséché pour application en « campagne de masse » en Iran. - *Renoux, G. (Tunis):* Préparation du vaccin antivariolique. Suppression des microbes de contamination secondaire et étalonnage. - *Mégias, J. et Moreno de Vega, F. et A. (Madrid):* Expérience de 30 années avec un virus dermique du vaccin contre la variole; données cliniques et expérimentales au sujet du même virus cultivé dans l'embryon de poulet.

Typhoid Vaccine. *De Barbieri, A. (Milan):* Chimica e biochimica degli antigeni tifici. - *Grasset, E. (Geneva):* L'appréciation de l'activité des vaccins antityphoïdiques par les résultats comparés des méthodes de titrage *in vitro* et *in vivo*. - *Grahbar, J. (Paris):* Epreuves de virulence et de séro-protection sur l'embryon de poulet. - *Ikli, D. (Zagreb):* Problems of standardization and control of typhoid fever vaccines. - *Eidvall, G. (Washington):* Reconsideration of methods for estimating the potency of typhoid vaccin. - *Giovanardi, A. (Milan):* Apprezzamento dell'attività del vaccino antitifico all'acetone. - *Didenko, S. I. (Moscow):* Problema biologiceskikh standartov pri kontrole effektivnosti protivotifosnoi baktisiny v eksperimente. - *Raus, K., Joó, I. and Réthy, L. (Budapest):* Preparation, control, results and perspectives of the adsorbed typhoid vaccine. - *Bonnefoi, A. (Paris):* De l'utilisation des diverses méthodes de titrage pour l'appréciation de l'activité d'un vaccin antityphoïdique. De l'opportunité d'une standardisation. - *Houbba, V. et al. (Praga):* Some new aspects on the control methods of strains and vaccine of S. typhi and S. paratyphi in submerged cultivation. - *Olitzki, A. L. and Artman, M. (Jerusalem):* The Vi- and O-antibody nitrogen content of rabbit immune sera produced with different types of typhoid vaccine compared with their agglutinating and protecting power. - *Djoridisti, M. et Drndarsky, K. (Belgrade):* Démonstration expérimentale sur la valeur immunisante du vaccin Salmonella typhi et S. paratyphi A et B chauffé ou alcoolisé. *Bonomini, G. e Gabrilli, G. (Pisa):* Il problema del controllo dei vaccini antitifici. La valutazione della loro attività mediante i tests di protezione attiva e passiva. - *Harris, E. (Lyon):* Préparation et contrôle d'un vaccin solubilisé et purifié contre la typhoïde. - *Matijouska, D. and Jelenc, J. (Praga):* On the question of experimental evaluation of typhoid vaccines. - *Ikli, D. (Zagreb):* The active mouse-protection test without mucin as a method for the potency test of typhoid vaccines.

Recommendations.

III

Proceedings of the Third International Meeting of Biological Standardization

Opštija 1957 (September 2-6) (Ed. Tiskara, Jzdavačkog zavoda Jugoslavenske akademije, 1958)

The Use of the Tissue Cultures in Vitro in the Control of Sera and Vaccines. *Penzo, G. and Vicari, G. (Rome):* Immunological phenomena studied by the tissue culture method. - *Evans, D. G. and Sansa, C. A. P. (London):* The action of Diphtheria toxin in tissue cultures and its neutralization by antitoxin. - *Vetš, I., Backhaus, R. and Horvath, I. (Budapest):* Investigation of Clostridium welchii, septicum and oedematis toxins in tissue cultures. - *Dislon, T. (Jerusalem):* The susceptibility of the developing of chick embryo to Diphtheria toxin and its use in titration of antitoxin. - *Mackowiak, C. et Lang, R. (Lyon):* Emploi des cultures de tissus dans le titrage du virus apteux et la recherche des anticorps. - *Lucam, F. et Mackowiak, C. (Lyon):* Résultats du contrôle et de l'application des vaccins antiphtéux en France. - *Nicol, L. et al. (Paris):* Essais de titrage sur œuf embryonné du virus de Carré, et d'un antisérum hyperimmun.

Influenza Vaccines. *Andrews, C. H. and Isaacs, A. (London):* Antigenic variation amongst Influenza viruses in relation to the production, use and standardization of vaccines. - *Svi-Moldavsky, G. J. (Moscow):* Perspectives of standardization of Influenza virus antigens by means of monospecific antisera, whose preparation is based on acquired immunological tolerance. - *Tang, F. F. and Liang, Y. K. (Peking):* Antigenic studies of Influenza virus isolated from the 1957 epidemic in China. - *Smorodintsev, A. A. (Leningrad):* A living anti-influenza vaccine and anti-influenza serum for influenza prophylaxis and treatment. - *Pontecorvo, M. (Napoli):* Adjuvants in immunization with influenza vaccines. - *Jový, J., Tumorá, B. et Radkovský (Praga):* L'emploi du sérum immun de cheval dans la prophylaxie de la grippe. - *Horváth, S. (Szeged):* Some methodical problems concerning virus titration and serum neutralization tests. - *Davoli, R. and Bartolacci-Corsi, O. (Florence):* Antibody response of man to intranasal administration of formal-killed influenza virus vaccine. - *Hennberg, G. (Berlin):* Aluminium hydroxide and aluminium oxide as deposit agents in influenza vaccines. - *Falcetti, E. (Siena) et Mériaux, C. (Lyon):* Essais d'immunisation chez le cheval contre le virus de la grippe.

Combined Vaccines. *Barr, M. (Beckenham):* The preparation, composition and control of combined vaccines. Combined vaccines containing tetanus toxoid. - *Scheibel, I. (Copenhagen):* Control of the Danish combined diphtheria-tetanus vaccine with special reference to the assaying of its antigenic potency in international units. - *Holt, L. B. (London):* Some pitfalls in the biometry of mixed antigens. - *Kluva, N., Fradkina, R., Sidorova, N. et Davidov, D. (Moscow):* Les vaccins combinés, leur composition, préparation et contrôle. - *Raus, K., Joó, I., Kétyi, I. and Réthy, L. (Budapest):* Preparation and control of combined typhoid-dysentery-tetanus vaccine and investigations into its immunogenic effect. - *Úngar, J. (Greenford):* Preparation, composition and control of combined vaccine. - *Mériaux, J. (Lyon):* Sur la possibilité de pratiquer en une seule intervention la première injection de vaccin contre la poliomyélite et la vaccination de rappel contre le tétanos. - *Mériaux, C. (Lyon):* Essai de simplification dans le rythme des vaccinations chez l'enfant. - *Regamey, R. H. (Bern):* Détermination rapide de la fraction tétanique dans les vaccins associés. - *Joó, I. and Réthy, L. (Budapest):* Preparation, standardization and control of combined diphtheria-tetanus-pertussis vaccines in Hungary. - *Regamey, R. H. (Bern):* Titrage rapide de la fraction diphthérique des vaccins associés, en particulier par la méthode de neutralisation de l'hémotoxine (phénomène de Seemüller). - *Réthy, L., Joó, I. and Kétyi, I. (Budapest):* Preparation and potency test of differently composed combined typhoid-tetanus vaccines. - *Ikli, D. (Zagreb):* Standardization of combined antigens. - *Cherif, J. et al. (Garches, Seine):* Etude comparative de vaccins triples antidiphthérique, antitétanique et anticoquelucheux simples et adsorbés.

Brucellosis Vaccines. *Gargani, G.* (Florence): Experiences performed at Italian brucellosis center about a killed, adsorbed, anti-Br. melitensis vaccine. - *Renoux, G.* (Tunis): Préparation et contrôle de quelques vaccins applicables aux brucelloses animales. - *Teklinski, A.* (Warsaw): Préparation et contrôle du vaccin anti-brucellose à partir de la souche S. 19. - *Olitzki, A. L. and Sulitzganu, D.* (Jerusalem): The antigenic structure in the genus *Brucella*.

Sterility Tests of Sera and Vaccines. *Bommel, P. H. et Raby, C.* (Clamart, Seine): Le contrôle de la stérilité des produits biologiques au moyen de milieux semi-liquides permettant la culture simultanée des aérobies et des anaérobies. - *Didenko, S. I.* (Moscow): Sterility control of sera and vaccines in the USSR. - *Scheibel, I. and Weiss Bentzon, M.* (Copenhagen): Sterility control of sera and vaccines. - *Benković, J. and Hig-Mandić, L. J.* (Zagreb): Sterility tests of immunobiological preparations.

Round Table Communications and Discussions. *Mérienne, C.* (Lyon): Projet des statuts pour l'Association des instituts producteurs de sérums et vaccins. - *Le Bourdellès, B. et Desbordes, J.* (Paris): Projet de classification des produits immunobiologiques et biologiques. - *Le Bourdellès, B. et Desbordes, J.* (Paris): Etude comparative des dispositions réglementaires relatives aux techniques de contrôle des préparations immunobiologiques dans quelques pays d'Europe.

Tetanus. *Fisek, N. H.* (Ankara): The immune response of men to fluid tetanus toxoids. - *Fisek, N. H. and Ertugrul, S.* (Ankara): Standardization of the small-pox vaccine by 6-point parallel line assay in the skin of the rabbits. - *Nicol, L. et al.* (Garches, Seine): Sur l'étude comparée de la valeur antigénique des anatoxines par la méthode de floculation et par la méthode du pouvoir de combinaison. - *Nicol, L. et al.* (Garches, Seine): Sur les contrôles subis par les antitoxines et anatoxines au cours de leur préparation. - *Ikit, D.* (Zagreb): Amount of A.U. in humans one year after vaccination with two anti-tetanus preparations of different potency.

Typhoid. *de Barbieri, A., Secova, M. E. and Benzioni, G.* (Milan): Isolation of endotoxins from *Salmonella paratyphi A* and *B*: their protective activity against the specific experimental infection. - *Pontecorvo, M.* (Naples): Preparation of formal killed typhoid vaccine retaining Vi antigenicity. - *Djurisic, M. et Drndarski, K.* (Belgrade): Problème de durée des agglutinines chez les cobayes vaccinés avec le vaccin Ty chauffé et alcoolisé. - *Benzoni, G.* (Milan): Effect of various agents on the immunizing activity of purified Vi antigen. - *Kluwa, N.* (Moscow): L'antigène Vi en qualité de test de contrôle de vaccin combiné. - *Ikit, D.* (Zagreb): Further research on the mouse-protection test without mucin as a method for the investigation of typhoid vaccines. - *Smorodintsev, A. A.* (Leningrad): Specific prophylaxis and treatment of influenza.

Recommendations.

IV

Proceedings of the Fourth International Congress for Biological Standardization

Bruxelles 1958 (24-30 juillet) (Ed. Imprimerie de Charleroi, Charleroi 1959)

Staphylococcal Vaccines. *d'Antona, D.* (Siena): L'anatoxine staphylococcique en médecine humaine. (Bases doctrinales, préparation, contrôle et applications pratiques). - *Goret, P.* (Alfort): Introduction à l'étude des staphylococcies. - *Richou, R.* (Paris): L'anatoxithérapie staphylococcique en médecine vétérinaire. - *Vygodtchikov, G.* (Moscow): Appréciation comparée des propriétés immunogènes de l'anatoxine staphylococcique et du vaccin staphylococcique. - Discussion: *d'Antona, D.* (Siena) - *Bonnefoi, A.* (Paris) - *Djurisic, M.* (Belgrade) - *Goret, P.* (Alfort) - *Regamey, R. H.* (Bern) - *Richou, R.* (Paris) - *Sobier, R.* (Lyon) - *Sorcia, S.* (Montreal) - *Vygodtchikov, G. V.* (Moscow).

Pyrogens and Their Control. *Van Genderen, H.* (Utrecht): Pyrogens, their mechanism of action and a few remarks on testing procedures. - Discussion: *Regamey, R. H.* (Bern) - *Van Genderen, H.* (Utrecht).

Control of Phage's Products. *Penso, G. et Ortolì, V.* (Rome): Le contrôle des produits thérapeutiques à base de phages. - Discussion: *Ahuja, M. L.* (London) - *Beumer, M.* (Bruxelles) - *Delville, J.* (Elisabethville) - *Djurisic, M.* (Belgrade) - *Hertzberger, E.* (Weesp) - *Nivolle, P.* (Paris) - *Penso, G.* (Rome) - *Sobier, R.* (Lyon).

Control During the Production. *Perry, W. L. M.* (London): Introductory report on the importance of control during production as compared with control of finished products. - *Regamey, R. H.* (Bern): Introduction aux contrôles en cours de production des substances immunobiologiques. - *Ikit, D.* (Zagreb): General observations on the production control of sera. - *Haas, R.* (Freiburg i.B.): Contrôle en cours de production du vaccin poliomyélique. - Discussion: *Ahuja, M. L.* (London) - *Ikit, D.* (Zagreb) - *Mielis, H.* (Warsaw) - *Perry, W. L. M.* (London) - *Regamey, R. H.* (Bern) - *Ungar, J.* (Greenford). - *Feinberg, J. G.* (Bethworth): Specific titration of biological solutions in agar gel plates. - Discussion: *Frenkel, H. S.* (Amsterdam) - *Feinberg, J. G.* (Bethworth). - *Henneberg, G.* (Berlin): Investigations on the filtration of virus suspensions.

Control of Vaccines in Veterinary Medicine. *Hulse, E. C.* (Weybridge): The production controls of living brucella vaccines, with special reference to strain 19 vaccine. - *Zavagli, V. et al.* (Rome): Le virus aphteux en culture de tissus (cellules rénales) dans la production et le contrôle des vaccins antiaphteux. - *Lang, R., Mackowiak, C., Petermann, H. G. et Fontaine, J.* (Lyon): Applications de la séro-neutralisation sur culture de tissu au contrôle du vaccin antiaphteux. - *Lucam, F. et Fedida, M.* (Lyon): Une nouvelle méthode quantitative pour l'appréciation de l'immunité antiaphteuse. - Discussion: *Falchetti, E.* (Siena) - *Hulse, E. C.* (Weybridge) - *Leunig, J.* (Uccle) - *Mackowiak, C.* (Lyon) - *Regamey, R. H.* (Bern) - *Renoux, G.* (Montpellier) - *Schoenacs, F.* (Bruxelles) - *Ungar, J.* (Greenford) - *Willms, R.* (Bruxelles) - *Zavagli, V.* (Rome).

Vaccinations for Children. *Mande, R., Herrault, A. et Lévy-Marchal, C.* (Paris): Les injections de rappel de vaccin dans l'enfance. - *Djurisic, M.* (Belgrade): L'effet de certains vaccins sur l'effet immunogène du vaccin B.C.C. - *Mérienne, C.* (Lyon): Sur l'association des anatoxines au vaccin antipoliomyélique et la simplification du calendrier des vaccinations. - *Rausz, K., Réthy, L., Kéty, K. et Marozzi, J.* (Budapest): Recherches sur l'effet immunisant des antigènes téaniques et dysentériques combinés à des antigènes «à l'action de rappel». Recherches sur le terrain. - *Rausz, K., Réthy, L., Kéty, I. et Jód, I.* (Budapest): Le rôle de l'intervalle entre les vaccinations par des vaccins polyvalents antidyentériques et par des vaccins combinés antityphoidiques-antidyentériques-anti-tétaniques. - *Backhaus, R., Veres, G. et Veto, I.* (Budapest): Nouvelle méthode d'hémagglutination passive pour le dosage des antitoxines et des anatoxines diphtériques. - Discussion: *Bonnefoi, A.* (Paris) - *Hertzberger, E.* (Weesp) - *Holt, L. B.* (London) - *Mande, R.* (Paris) - *Rafiy, A.* (Tehran) - *Sobier, R.* (Lyon) - *Ungar, J.* (Greenford).

Tuberculine. *Desbordes, J.* (Paris): Rapport sur la tuberculine. Projet de contrôle international de la tuberculine. - Discussion: *Brety, J.* (Paris) - *Martin, L.* (Bruxelles).

Live Vaccines. *Sobier, R.* (Lyon): Introduction à l'étude du contrôle des vaccins «vivants». - *Brety, J.* (Paris): Les contrôles d'innocuité du B. C. G. - *Sobier, R., Freydis, J. et Challa-Thal, F.* (Lyon): Etude de la réaction de fixation du complément au cours de la grippe asiatique. Influence de l'âge des sujets sur l'élaboration des anticorps réagissant aux différents antigènes «solubles» ou «viraux» du groupe A (PR 8) et A (ASIE 57). - *de Somer, P., de Maeyer, E. et Prinzie, A.* (Louvain): Description d'un test d'antigénicité du vaccin antipoliomyélitique. - *Frenkel, H. S.* (Amsterdam): Deux méthodes de culture du virus vaccinal sur tissu en survie. - *Hauduroy, P. et Paccard, M.* (Lausanne): Etude de l'effet cytopathogène de la toxine diphtérique sur les cellules cancéreuses HeLa et KB et sur les cellules rénales simiennes. - Discussion: *Catigne, G.* (Paris) - *Sobier, R.* (Lyon) - *Ungar, J.* (Greenford).

Sterility. *Bonnel, P. H. et Rahy, C.* (Clamart, Seine): Résultats d'un an d'application des recommandations de la 3^e R.I.S.B. (Opatija, 2-6 septembre 1957) sur les contrôles de stérilité des sérums, vaccins et autres produits immunologiques.

Documentation and Bibliography. *Brygoo, P. R. et Meyer, P.* (Paris): La standardisation de la documentation en microbiologie et immunologie. - Discussion: *Brygoo, P. R.* (Paris) - *Haugard, S.* (Bruxelles) - *Renoux, G.* (Montpellier). - *Le Bourdillat, B. et Desbordes, J.* (Paris): Projet de classification des produits immunologiques et biologiques. - Discussion: *Bonnel, P. H.* (Clamart, Seine). - *Hauduroy, P.* (Lausanne): Le rôle du Centre international de collections de cultures dans la standardisation biologique. - Discussion: *Sobier, R.* (Lyon). - *Martin, L.* (Bruxelles): Aspects biométriques du titrage de substances anticoagulantes.

Conclusions and Resolutions. Conclusions of the 4th International Congress for Biological Standardization. Brussels, 24-30 July 1958. - Regulations of the International Society for Biological Standardization (later: Permanent Section for Microbiological Standardization).

V

5th International Meeting of Biological Standardization

Jerusalem 1959 (September 13-20) (The Weizmann Science Press of Israel, Jerusalem 1960)

Standardization of Prophylactics and Diagnostics in Human Virus Infections. *Heller, L.* (Stockholm): Potency testing and standardization of killed influenza vaccines (some problems involved). - *Benenson, A. S.* (Washington): Evaluation of dried smallpox vaccine. - *Kreth, U., Schoeb, H. and Wulff, H.* (Bern): The evaluation of smallpox vaccine in tissue cultures and eggs. - *Berikopf, H. et al.* (Jerusalem): Antibodies to trachoma virus. - Discussion: *Babudieri, B.* (Rome). - *Bernkopf, H., Nishimi, M. and Katzenelson, E.* (Jerusalem): Use of mouse macrophage cultures for the determination of the toxicity of viruses.

Standardization of Prophylactics in Zoonoses and Antropozoonoses Caused by Viruses. *Goret, P., Vacher, B. et Michal, C.* (Alfort): Le titrage des sérums spécifiques des virus animaux; nécessité d'une standardisation des techniques. - Discussion: *Rafii, A.* (Teheran). - *Sartorius, F. and Winkler, C.* (Potsdam): Bemerkungen und Untersuchungen zur Gewinnung, Wertbestimmung und Anwendungsweise von Rabidien Immunsren. - *Goldwasser, R. A. and Kimron, A.* (Ness-Ziona): Time of appearance of rabies virus antigen in brains of mice following inoculation of the virus. - *Lucam, F. et Fedida, M.* (Lyon): Une méthode quantitative d'appréciation de l'immunité antiptreuse. - *Mackowiak, C. et al.* (Lyon): Application au contrôle du vaccin antiptreux de la séro-neutralisation sur cellules rénales.

Inactivated Poliomyelitis Vaccines. *Penso, G.* (Rome): Report of an international collaborative assay on the potency of inactivated poliovaccine. - *Murray, R.* (Bethesda, Md.): The potency of inactivated poliomyelitis vaccine. - *Lépine, P., Roger, F., Sautter, V. et Roger, A.* (Paris): Application de la réaction cinétique de séro-neutralisation à l'étude de l'antigénicité des vaccins antipoliomyélitiques (Méthode de l'Institut Pasteur). - *Prinzie, A., de Somer, P., Lawry, M. et de Maeyer, E.* (Louvain): La détermination de la valeur antigénique du poliovaccin. - *Gerwe, E. G.* (Indianapolis, Ind.): Testing of antigenicity of poliomyelitis vaccine. - *Berger, E.* (Basel): Intensity and persistence of serological immune reactions against poliomyelitis virus after vaccination with Salk's vaccine. - *Benesh-Melnick, M. and Melnick, J. L.* (Houston, Tex.): Neutralizing antibody combining (NAC) test for measuring antigenic potency of poliomyelitis vaccine. - *MacLeod, D. R. E. et al.* (Toronto): Poliovirus antibody response following various vaccination schedules and at different ages. - *Gottlieb, T. and Leventon, S.* (Tel Aviv-Yafo): Use of an *in vitro* method for the determination of the antigenic potency of formalinized poliomyelitis vaccine. - *Fogel, A. et al.* (Tel Aviv-Yafo): Antigenicity of formalinized poliomyelitis vaccines (Salk type) as measured in laboratory animals and triply negative infants. - *Spigland, I., Goldblum, N., Skalska, P. and Muchnicka, D.* (Tel Aviv-Yafo): Serologic response of young infants to Salk vaccine: a preliminary report.

Living Poliomyelitis Vaccines. *Cabuso, V. J. and Cox, H. R.* (Pearl River, N.Y.): Proposed testing requirements for oral poliomyelitis vaccine. - *Melnick, J. L. and Benesh-Melnick, M.* (Houston, Tex.): Studies on live poliovirus vaccine and its increased neurovirulence after multiplication in vaccinated children.

Combined Vaccinations. *Mirieux, C.* (Lyon): Poliomyélite et vaccinations associées. - *Desbordes, J.* (Paris): Note sur le contrôle de l'association du vaccin antipoliomyélitique avec le vaccin antioquelucheux et les anatoxines diphtérique et tétanique. - *Pontecorvo, M.* (Naples): Control of the efficiency of multiple antigen against poliomyelitis, diphtheria, pertussis and tetanus. - *Ritly, L.* (Budapest): Premiers résultats de la réactivité de vaccination associée contre la diphtérie, le tétanos, la coqueluche et la poliomyélite en Hongrie. - *Wilson, R. J., Moss, G. W. O., Potter, F. C. and MacLeod, D. R. E.* (Toronto): Diphtheria and tetanus toxoids combined with pertussis and poliomyelitis vaccines. - *Wilson, R. J.* (Toronto): Tetanus-polio vaccine. - *Bleick, K., Pansini, K., Kon, L. and Ikit, D.* (Rifeka): Reactions after combined inoculation against poliomyelitis, diphtheria, tetanus and pertussis (1st and 2nd doses). - Discussion: *Fedén, C. G.* (Stockholm).

General Problems, Precaution and Safety Tests. *Fisek, N. H.* (Ankara): The validity of biological products. - Discussion: *Borrel, A.* (Toulouse).

Standardization of Prophylactics and Diagnostics in Leptospirosis. *Babudieri, B.* (Rome): Vaccine against leptospirosis. - Supplement 1: Minimum requirements of leptospira vaccine in Japan (*Kitaoka, M.* / Tokyo) - Supplement 2: Criteria suggested for anti-leptospirosis vaccine for human use (The Metschnikoff Institute / Moscow) - Supplement 3: Control of anti-leptospirosis vaccine (Istituto Superiore di Sanità / Rome) - Supplement 4: Extracts of requirements for licensing Leptospira pomona bacterin (United States Department of Agriculture, Agricultural Research Service, Animal Inspection and Quarantine Division). - *Babudieri, B.* (Rome) and *van der Hoeden, J.* (Ness-Ziona): Proposals concerning the preparation of leptospira vaccines. - *Van der Hoeden, J.* (Ness-Ziona): Standardization of laboratory procedures in the diagnosis of leptospirosis. - *Eylan, E.* and *Schwarz, Z.* (Tel Aviv): Complement fixation studies with leptospiras.

Precipitation in Agar Gels. *Feinberg, J. G.* (Bethworth): Titration and assay of toxins, toxoids and antitoxins in quantitative agar gel precipitation plates. - *Braun, W., Plescia, O. J.* and *Palczuk, N. C.* (New Brunswick, N.J.): Studies with DNA-associated antigens of *Brucella abortus*. - *Olitzki, A. L., Markenson, J.* and *Margalit, M.* (Jerusalem): Studies on the active immunization of mice against experimental *Brucella* infections by DNA-conjugated proteins and passive protection tests by anti-DNA-immune sera. - *Eylan, E., Imre, C.* and *Keydar, J.* (Tel Aviv-Yafo): Studies on the antigenic structure of *Corynebacterium diphtheriae* with the aid of agar gel precipitation technique. - Discussion: *Gargani, G.* (Florence). - *Bouquet, P.*: I. Proposals on the use of agar gel methods for biological standardization. - *Feinberg, J. G.* (Bethworth): II. Proposals on the use of agar gel methods for biological standardization.

Standardization of Bacterial Prophylactics and Diagnostics. *Gargani, G.* (Florence): Standardization of control methods of anti-brucellosis vaccines. - *Janovic, A.* (Johannesburg): The influence of antitoxin immunity on the cellular response to staphylococcal infection in rabbits. - *Johannovsky, J.* (Praha): Some problems of staphylococcal infection. - *Wilson, R. J., Fremes, A.* and *Corkill, J. M.* (Toronto): Report on clinical trials of staphylococcus toxoid (86 patients). - *Sterne, M.* (Beckenham): The standardization of *Clostridium perfringens* and *Clostridium botulinum* sera and vaccines. - Discussion: *Krag, P.* (Copenhagen). - *Ungar, J.* (Greenford): The control of the efficiency of freeze-dried BCG vaccine. - Discussion: *Breley, J.* (Paris) - *Krag, P.* (Copenhagen) - *Blagovicheski, S.* (Moscow). - *Parnas, J.* (Lublin): The standardization of some allergens employed in the diagnosis and therapy of anthropeozonoses.

Antigens of Parasitic Origin. *Coudert, J.* (Lyon): Antigènes parasitaires lyophilisés.

C-Reactive Protein. *Gal, K.* and *Miltényi, M.* (Budapest): Haemagglutination test for the demonstration of C-reactive protein. *Böszörményi, J.* (Budapest): Nouvelles données sur la méthode de détermination de la «proteine C-reactive». - *Rozansky, R., Havini, Y.* and *Hermoni, D.* (Jerusalem): Determination of C-reactive protein by precipitation and complement fixation methods.

Passive Haemagglutination. *Berger, E.* and *Bauer, R.* (Basel): The haemagglutination test as a method for the quantitative determinations of antibodies against food-antigens. - *Fleck, L., Porath, S.* and *Evenshik, Z.* (Ness-Ziona): Inhibition of passive haemagglutination as a method for detection of antigenic substances.

Antivenomous Immune Sera. *Boquet, P.* (Garches): Sur l'uniformisation des méthodes de mesure de l'action antitoxique des sérums thérapeutiques antivenimeux. - Discussion: *Shulov, A.* (Jerusalem). - *Kochwa, S. et al.* (Petach Tiqva): Production of antibodies against *Viper a xanthina* palestinae venom and venom fractions. - Discussion: *Shulov, A.* (Jerusalem). - *Shulov, A. et al.* (Jerusalem): The anti-scorpion serum prepared by use of fresh venom and the assessment of its efficacy against scorpion stings.

Conclusions. List of Participants. - Rules of the Permanent Section for Microbiological Standardization.

VI

Proceedings of the 6th International Congress of Microbiological Standardization

Wiesbaden 1960 (September, 5-10) (H. Hoffmann Verlag, Berlin-Zehlendorf 1961)

Polio Vaccine, Oral. *Sabin, A. B.* (Cincinnati, Ohio): Testing and Standardization of Live Polio Vaccines. - *Murray, R.* (Bethesda, Md): Recommendations relating to the Manufacture of Poliovirus Vaccine, Live, Oral. - *Chumakov, M. P. et al.* (Moscow): Problems of Manufacture and Control of Live Poliovirus Vaccine from A. B. Sabin's attenuated Strains. - *Plotkin, S. A.* (Philadelphia, Pa): Factors influencing a successful Vaccination with Live Polio Virus. - *De Somer, P., Prinzie, A. et Lahy, M.* (Louvain): Le contrôle du vaccin antipoliomyélique. - *Ritly, L. et al.* (Budapest): Simultan-Impfung: Polio-Lebendvakzine und DTP-Adsorbat. - *Starke, G.* and *Welke, G.* (Berlin): Erfahrungen bei der Titerkontrolle attenuierter Polioviren mittels permanenter Zellstämme. - *Okuno, Y.* (Osaka): Studies on Attenuation of Virulence of Poliovirus (Type I, Brunhilde strain) by serial Passage in developing Chick Embryo. - Discussion and Resolution: *Henneberg, G.* (Berlin) - *Hennessen, W.* (Marburg/L) - *Kleinschmidt, H.* (Honnaf) - *Krag, P.* (Copenhagen) - *Murray, R.* (Bethesda, Md) - *Slonim, D.* (Praha) - *Stojkovic, L.* (Belgrade).

Combined Polio Vaccines. *Wilson, R. J.* and *MacLeod, D. R. E.* (Toronto): Mutual Influence of Antigens in combined Vaccines (Di-Tet-Pert-Pol.). - *McLean, I. W. Jr.* and *Timm, E. A.* (Detroit, Mich.): Clinical Trials of a quadruple Antigens (DTP a. Polio) in Infants of varying Age. - *Hennessen, W., Mauler, R.* and *Körner, L.* (Marburg): Potency testing with combined Polio Antigens. - *Zourbas, J. et Leclainche, X.* (Paris): Vaccination antipoliomyélique dans les crèches du Département de la Seine (1958-1960). - *Drescher, J.* (Berlin): Experimente über die Beziehungen zwischen Antigenzufuhr und Antikörperbildung bei Kombinationsimpfstoffen. - Discussion and Resolution: *Desbordes, J.* (Paris) - *Feinberg, J. G.* (Bethworth) - *Henneberg, G.* (Berlin) - *Hennessen, W.* (Marburg) - *McLean, I. W.* (Detroit, Mich.) - *Murray, R.* (Bethesda, Md) - *Nicol, L.* (Paris) - *Roger, F.* (Paris) - *Ungar, J.* (Greenford) - *Wilson, R. J.* (Toronto).

Measles. *Goffe, A. P.* (Beckenham): Prospects in the Prophylaxis of Measles. - *Gore, P.* (Alfort): Sur les relations croisées des caractères pathogènes, antigènes et immunogènes des virus de la rougeole, de la Maladie de Carré et de la peste bovine et sur le rôle du chien dans la transmission d'infections virales à l'homme. - *Imagawa, D. T.* (Los Angeles) and *Adams, J. M.*: Measles, Distemper and Rinderpest-Complex. - *Frankel, J. W.* (Norristown, Pa.): Studies on Isolates of Measles Virus and Responses to Vaccination with inactivated Measles Virus Vaccines. - *Okuno, Y.* (Osaka): Studies on the Prophylaxis of Measles with attenuated and inactivated Measles Virus. - Discussion and Resolution: *Enders-Ruckle, G.* (Marburg/Lahn) - *Heller, L.* (Stockholm) - *Henneberg, G.* (Berlin) - *Honwink* (Weesp) - *Imagawa, D. T.* (Los Angeles) - *Mérienx, C.* (Lyon) - *Rott, R.* (Tübingen).

Germ Counting. *Hulse, E. C., Hopkins, I. G. and Hebert, C. N.* (Weybridge): A Comparison between the dropping Pipette and the graduated Pipette Techniques for the Viability Counting of bacterial Suspensions. - *Jod, I.* (Budapest): Significance of bacterial Count in the Preparation and Potency Test of Vaccines. - *Ollitzki, A. L.* (Jerusalem): The Determination of the Number of Microorganisms in a bacterial Suspension. - *Ungar, J.* (Greenford): The Evaluation of B. Pertussis Suspensions. - *Panisset, M. et Benoit, J. C.* (Montreal): Numération des unités viables et numération totale des cellules dans les suspensions de bacilles tuberculeux et, en particulier de BCG. - *Ikit, D.* (Zagreb): The Role of the Number of Germs in the Control of Vaccines prepared from killed Germs (Typhoid Vaccine, Pertussis Vaccine). - *Frank, H.* (Weihenstephan): Die volumetrische Keimzahlbestimmung und ihre Vorteile gegenüber anderen Methoden. - Discussion and Resolution: *Candido de Oliveira, J.* (Lisbon) - *Hulse, E. C.* (Weybridge) - *Reber, H.* (Basel)

Desinfection. *Desbordes, J. et Le Bourdellès, B.* (Paris): Etudes des procédés de contrôle d'efficacité des antiseptiques utilisés pour la désinfection des locaux. - *Fust, B.* (Basel): Evaluation of bactericidal Disinfectants. - *Droubet, E.* (Paris): L'évaluation des antifongiques pour les essais thérapeutiques des mycoses humaines et animales. - *Drees, O.* (Hamburg): Evaluation of virucidal Properties of Disinfectants. - *Phillips, C. R.* (Ft. Detrick, Md): Limitations of standard Methods for testing Disinfectants. - *Tartler, G. and Theus, P. M.* (Greiswald): Zur Raumluftentkeimung durch Luftfiltration. - *Bueker, K.* (St. Gallen): Beobachtungen betreffend den Sterilisierungseffekt von Äthylenoxyd-Kohlendioxid-Gemischen bei Bakterien und Bakteriensporen. - Discussion and Resolution: *Dony, J.* (Brussels) - *Damm, H.* (Düsseldorf).

Veterinary Matters. *Stableforth, A. W.* (Weybridge): The proposed international Standard for Newcastle Disease Vaccine. - *Panisset, M. et Marois, P.* (Montreal): Contrôle vétérinaire et microbiologique d'un vaccin buvable contre la Maladie de Newcastle. - *Eisner, G.* (Frankfurt a/M): Standardisierung von Vaccinen gegen die atypische Geflügelpest (Tot-Vaccine). - *Goret, P., Vacher, B., Fontaine, J. et Mackowiak, C.* (Alfort et Lyon): Préparation et titrage du sérum contre la Maladie de Carré. - *Lucas, F. et Fédida, M.* (Lyon): Standardisation des vaccins antiptéux par la méthode de d'indice de protection K₅₀. - *Lang, R. et al.* (Lyon): Standardisation d'une méthode de contrôle du vaccin antiptéux. - Discussion and Resolution: *Fritzsche, K.* (Koblenz) - *Goret, P.* (Alfort) - *Haas, R.* (Freiburg) - *Korb, J.* (Prahá) - *Orfei, Z.* (Rome) - *Pappe, H. H.* (Bremen) - *Reculard, P.* (Garches) - *Vallée, A.* (Paris).

Rules of the Permanent Section for Microbiological Standardization.

Ikit, D. (Zagreb): The present State and Problems of microbiological Standardization.

VII

Proceedings of the 7th International Congress for Microbiological Standardization

London 1961 (August 28 to September 1) (E. & S. Livingstone Ltd., Edinburgh and London 1962)

Biological Standardization. *Jerne, N. K.* (WHO, Geneva): International biological Standardization. - *Evans, D. G.* (London): International and national biological Standards and Reference Preparations. *Krag, P.* (Copenhagen): Biological Standards and Reference Preparations: their Preparation, Establishment and distribution. - *Stableforth, A. W.* (Weybridge): Standards of veterinary Interest.

The Use of Standards. *Regamey, R. H.* (Genève): Comment simplifier les contrôles officiels des produits immunologiques. - *Barr, M.* (Beckenham): Laboratory Standard Antitoxins and Toxoids. - *Fauchet, S., Triant, R. et Dubreuil, P.* (Lyon): Problèmes concernant l'utilisation de quelques étalons biologiques. - *Sterne, M.* (Beckenham): The protective Value of veterinary clostridial Antisera and Vaccines. - *Weig, B.* (Elstree): Variations in the Assay of Tetanus Antitoxin. - *Batty, I.* (Beckenham): The Use of Mice in the Standardization of Veterinary anaerobic Vaccines. - *Joubert, L. et Biéranger, G.* (Lyon): Un nouveau mode de titrage biologique statistique de standardisation internationale: le «titre-temps», en unités «néoprobis», de virulence, de toxicité ou d'immunité. - *Mérieux, C. et al.* (Lyon): Standardisation biologique des gammaglobulines. Proposition pour une préparation de référence. - *Kolosev, S. G.* (Moscow): Problems of the Standardization of veterinary biological Products in the U.S.S.R. - *Houba, V.* (Prahá): Some Aspects of the Standardization of some Enzyme Preparations.

International Standards. *Ikit, D.* (Zagreb): The Application of biological Standards and Reference Preparations in international and national Requirements for biological Products. - *Bangham, D. R.* (London): International Standards in national Control. - *Hulse, E. C.* (Weybridge): The Application of international Standards in the national Control of veterinary biological Products.

Adventitious Agents in Tissue Cultures. *Greening, C. L.* (Beckenham): The controlled Collection, Holding, Transport and Stock Housing of Monkeys intended for Tissue Culture Production. - *Hiatt, C. W.* (Bethesda, Md): Differential Rate Methods for selective Inactivation of Viruses. - *Malverbe, H.* (Johannesburg): Viruses recovered from Cercopithecus Monkeys in South Africa. - *Pay, T. W. F.* (Sandwich): Some Observations on vacuolating Agent Virus (SV 40). - *Nagler, F. P.* (Ottawa): The Removal of adventitious Agents from live Poliovirus Vaccines.

Diagnostic Sera for Viruses. *Davie, J.* (Pirbright): Criteria for the serological Differentiation of sub-types of the Virus of Foot-and-Mouth Disease. - *Von Magnus, H., Godfredsen, A. and Munkel, B. S.* (Copenhagen): Specific hyperimmune Sera for Identification of Enteroviruses. - *Pascaud, M. F.* (Geneva): Le problème des antisérums et des antigènes en matière de diagnostic virologique. - *Bradstreet, C. M.* (Colindale): Problems associated with the Estimation of Potency of a neutralizing Serum for the Typing of Viruses. - *Buccia, M. and Winn, J. F.* (U.S.A.): General Problems relating to the Preparation of viral Diagnostic Antisera for Reference and Control Purposes.

Sterility Testing. *Proom, H.* (Beckenham): Sterility Test Regulations and the Manufacturer. - *Desbordes, J. et Ninard, B.* (Paris): Le point de vue du contrôleur et de l'expert dans l'essai de stérilité des produits utilisés en médecine humaine. - *Pittman, M. and Feeley, J. C.* (Bethesda, Md): Sterility Testing: Detection of fungal and Yeast Contamination in biological Preparations. - *Heden, C. G. and Markkula, H.* (Stockholm): A simple bacteriological Test for Sterilization Equipment. - *Lightbo, J. W.* (London): The Sterility Testing of Antibiotics.

Toxicity Testing. *Gerwe, E. G.* (Indianapolis, Ind.): Tests for non-specific Toxicity of Pertussis Vaccine. - *Holt, L. B.* (London): Some Observations on the Toxicity of Pertussis Vaccine.

Tuberculin Problems. *Magnusson, M. and Wijsmuller, G.* (Copenhagen): Standardization Problems concerning Tuberculin caused by the Use of Stabilizing diluent containing Tween 80. - *Lesslie, I. W. and Hebert, C. N.* (Weybridge): The Adsorption of Avian PPD Tuberculin to Glass. - *Fillastre, C. et Magloire, C.* (Paris): Les essais pratiques sur la tuberculine. - *Edsall, G. et al.* (Boston, Mass.): Guinea Pig VS. Man in Standardization of Tuberculin.

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Problems in Standardizing Protein Preparations

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With the development of biochemistry and immuno-biology of proteins the use of protein preparations became more and more extensive in the clinic for prophylaxis and therapy, as well as in the laboratory for testing purposes. Furthermore the requirements for control in production procedures of protein preparations have become very rigorous. The need for a guarantee of well defined quality characteristics stems from the demand of the user of protein preparations—either physician or laboratory worker—to obtain with such preparations reproducible effects.

Standardization and quality control of protein preparations depends on chemical and biological methods, whereby one can distinguish between the characterization by means of chemical and physico-chemical parameters—which I would like to call the *basic parameters*—and those parameters giving evidence of the reactive capacity contained in the preparations—i.e. the more *functional parameters*.

Basic Parameters

When dealing with the basic parameters of characterization the fundamental information—of course—concerns the *total nitrogen content* of a preparation.

One of the means of obtaining detailed knowledge of the preparation is *electrophoretic analysis*. In spite of the development of routine methods, free fluid electrophoresis remains the method of reference as can be seen from various Minimum Requirements for protein preparations. Free fluid electrophoresis must be applied under well defined experimental conditions—buffer quality, pH and ionic strength—in order to obtain comparable results. It is very useful for the overall control of purity, or for the distribution of fractions contained in a preparation (Fig. 1).

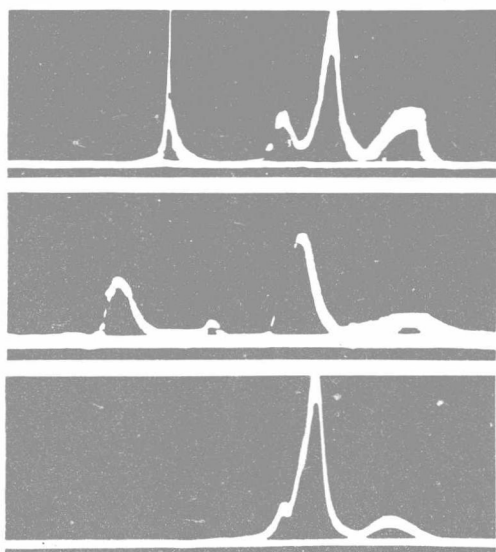


Fig. 1. Electrophoretic pattern of human fibrinogen preparations from three different sources.

Free fluid electrophoresis allows characterization of a given protein according to its mobility, i.e. the migration in the electrical field under standard conditions. But for finer description of the electrophoretic behaviour the determination of the dependance of the mobility on the pH may be useful in giving a curve with a specific slope and indicating the isoelectric point.

Since so much stress had been laid upon the electrophoretic purity, it seems worthwhile to briefly discuss the problem of electrophoretic purity versus functional capacity. In this respect the requirement of a mobility limit of $-2.8 \times 10^{-5} \text{ cm}^2 \text{ volt}^{-1} \text{ sec}^{-1}$ for gamma globulin does not appear in full concordance with the mobility classes of proteins in which antibodies can be found (Fig. 2).

Paper electrophoresis has the advantage of the simplicity of the apparative setup, but does not allow the direct determination of exact mobilities. Also the inequality of the avidity of the various protein fractions towards dyes is a drawback when the evaluation is done photoelectrically. Additionally paper electrophoresis is only a qualitative approach to the determination of the lipid and carbohydrate load of certain proteins. Starch gel electrophoresis by reason of the special qualities of the carrier medium appears promising for the future, when very fine analytical dissolution into minor components of a mixture is necessary.

Also widely used in purity control is the sedimentation analysis with the ultracentrifuge. As the criteria for separation into fractions of different sedimentation constants are chiefly the molecular weight and the partial specific volume; it may happen that the degree of purity found with electrophoresis is incongruent