THE SOCIETY OF THE PLASTICS INDUSTRY, INC.
250 PARK AVENUE • NEW YORK, NEW YORK 10017 • 212/687-2675

MINUTES

MEETING OF SPI FOOD, DRUG AND COSMETIC PACKAGING MATERIALS COMMITTEE

Summit Hotel of New York
New York, N. Y.

June 19, 1969
9:40 a.m.

Present:

Robert M. Miller, Chairman, Hercules, Inc., 910 Market St., Delaware Trust Bldg., Wilmington, Del. 19898
Taylor W. Hanavan, Vice Chairman, E. I. du Pont de Nemours & Co., Inc., 1007 Market St., Film Dept., Wilmington, Del. 19898
W. B. Ackart, Union Carbide Corp., Chemicals & Plastics, One River Road, Bound Brook, N. J. 08805
R. Arnold, M & T Chemicals Inc., Woodbridge Ave., Rahway, N. J. 07065
R. C. Asam, The Goodyear Tire & Rubber Co., Chemical Materials Dept., Dept. 480D, 1485 E. Archwood Ave., Akron, Ohio 44316
W. M. Atkinson, Nopco Chemical, 60 Park Place, Newark, New Jersey
N. D. Bornstein, W. R. Grace & Co., Cryovac Div., Duncan, S. C. 29334
K. C. Conley, Development Div., Borg-Warner Corp., Washington, W. Va. 26181
P. F. Cundy, American Can Co., Research & Development Dept., Box 702, Neenah, Wis. 54956
R. A. Dannells, Dart Industries, Inc., P. O. Box 37, Paramus, N. J. 07652
L. J. DeCorte, Sinclair-Koppers Co., Product Development, Frankfort Rd., Monaca, Pa. 15061
H. R. Dittmar, Imco Container Co., Div. Ethyl Corp., 75th & Cleveland Sts., Kansas City, Mo. 64132
D. S. Dixler, AIRCO, Air Reduction Co., Inc., Central Research Laboratory, Murray Hill, N. J. 07971
R. J. Dowling, Uniroyal Chemical, Div. of Uniroyal, Inc., Elm St., Naugatuck, Connecticut 06770
G. W. Ferner, The Goodyear Tire & Rubber Co., Research Div., 1144 East Market St., Akron, Ohio 44316
A. B. Finestone, Foster-Grant Company, Inc., 289 North Main St., Leominster, Mass.
S. W. Foulkrod, III, Law Division, Scott Paper Co., Research Div., Philadelphia, Pennsylvania 19113
L. J. Friedman, Ruco Division, Hooker Chemical Corp., New South Rd., Hicksville, New York 11802
B. J. Garceau, ICI America, Inc., P. O. Box 1274, 151 South St., Stamford, Conn.
Jerome H. Heckman, Keller & Heckman, 1712 "N" St., N. W., Washington, D.C. 20036
P. L. Henry, Esquire, Allied Chemical Corp., P. O. Box 405, Morristown, N. J.

K. A. Hochschwender, American Hoechst Corp., P. O. Box 2500, Somerville, N. J.
T. J. Hughes, Esquire, Keller & Heckman, 1712 "N" St., N. W., Washington, D. C.
D. H. Hunter, Stauffer Chemical Co., Plastics Div., P. O. Box 320, Delaware City, Delaware 19706
G. W. Ingle, Monsanto Co., 1101 - 17th St., N. W., Suite 604, Washington, D. C.
N. A. Jappe,Scott Paper Co., Philadelphia, Pennsylvania 19113
J. F. Jones, The Standard Oil Co. (Ohio), Midland Bldg., Cleveland, Ohio 44115
W. A. Knapp, Allied Chemical Corp., ~~Ind. Chemical Div.~~, P. O. Box 405, Morristown, N. J. 07960
F. S. Landers, Owens-Illinois, Lily Tulip Div., 500 Commack, N. Y. 11725
W. A. Larkin, M & T Chemicals, Inc., Rahway, New Jersey 07065
J. R. S. McCartney, Standard Packaging Corp., 111 Prospect St., Stamford, Conn.
J. McDermott, SPI, 250 Park Ave., New York, New York 10017
G. L. McIntyre, Columbian Carbon Co., P. O. Box 975, Princeton, N. J. 08540
K. Morgareidge, Food & Drug Research Laboratories, Inc., Maurice Ave. and 58th St., Maspeth, N. Y. 11378
P. Morison, Eastman Chemical Products, Inc., Chemical Sales Dev. & Technical Service, Kingsport, Tenn. 37662
W. P. Munro, American Cyanamid Co., Bound Brook, New Jersey 08805
B. G. Murray, Ferro Corporation, Color Division, 4150 E. 56th St., Cleveland,Ohio
S. Nesmith, USI Chemicals Co., P. O. Box 218, Tuscola, Ill. 61953
A. S. Nyquist, American Cyanamid Co., P. O. Box 425, South Cherry St., Wallingford, Conn. 06492
J. N. O'Connor, The Dow Chemical Co., Legal Dept., 47 Bldg., Midland, Mich. 48640
B. N. Olson, Reynolds Metals Co., 10th & Byrd Sts., Richmond, Va. 23219
I. F. Peake, E. I. du Pont de Nemours & Co., Inc., Film Dept., 1007 Market St., Wilmington, Del. 19898
G. A. Richter, Jr., Rohm & Haas Co., Independence Mall West, Philadelphia, Pa.
A. M. Schnitzer, Phillips Petroleum Co., Research & Development Dept., 356 Chemical Laboratories, Bartlesville, Okla. 74003
W. W. Sederlund, National Starch & Chemical Corp., 1700 West Front St., Plainfield, N. J. 07063
M. E. Smith, Owens-Illinois, Plastic Products Div., Adams & 14th Sts., Toledo,Ohio
C. J. Spiegl, Continental Can Co., Inc., 7622 South Racine Ave., Chicago, Ill.
M. C. Stone, Eastman Chemical Products, Inc., P. O. Box 431, Kingsport, Tenn.
V. R. Struber, Argus Chemical Corp., 633 Court St., Brooklyn, N. Y. 11131
M. F. Tietze, Airco Chemical & Plastics Div., Air Reduction Co., Inc., Murray Hill, N. J. 07971
H. Turpack, Diamond Shamrock Corp., P. O. Box 191, Painesville, Ohio 44077
W. M. Westveer, The Dow Chemical Co., 433 Bldg., Midland, Mich. 48640
A. G. Whitney, W. R. Grace & Co., Research Div., Clarksville, Md. 21029
Charles L. Condit, Secretary, SPI, 250 Park Ave., New York, N. Y. 10017

Robert M. Miller, Hercules, Inc., Chairman of the Committee, called the business session to order at 9:40 a.m. He then referred to a detailed agenda circulated with the Secretary's meeting announcement and, as a first order of business, asked for the usual self-introductions.

Minutes Last Meeting Approved

In the absence of comments as to corrections or additions to the Minutes of the last meeting held on November 7, 1968, Mr. Miller declared them approved as written and distributed by the Secretary.

Remarks of Committee Chairman

Mr. Miller then dealt briefly with several items of general interest to the Committee.

He, firstly, announced that James A. Mitchell, Film Department, E. I. du Pont de Nemours & Co., Inc., has within recent weeks retired from the company and then asked that the Secretary place in the records a statement of deep appreciation to Mr. Mitchell for the time and effort that he has expended during some ten years of membership on the Committee.

Mr. Miller next reported that within recent weeks, the American Society of Mechanical Engineers has organized a Food, Drug and Beverage Equipment Committee; that in this regard, SPI was invited to be represented on the Committee if it felt that it could contribute to the activities of the group. Continuing, Mr. Miller said that, essentially the purpose of the new committee, as presently defined at least, is to study the possibility of developing a safety code on food, drug and beverage equipment and practices. Mr. Miller then said that he instructed the Secretary to advise ASME that, at present, the SPI Committee is not immediately interested in equipment per se, but that the Society would indeed like to be on the mailing list of the ASME Committee so that we can be aware of its activities and perhaps take an active part in its future work if there are indications that this would be mutually beneficial. The Secretary has taken this step and the Society is now on the ASME group's list.

Continuing, Mr. Miller reminded that, under date of January 3, 1969, Jerome H. Heckman, Esquire, Keller and Heckman, had advised all members of the Committee about a communication received from Dr. Maurice Green of the American National Red Cross relative to a proposed protocol for a plastics evaluation program to be conducted by the Red Cross, the said program being designed to evaluate plastic materials suitable for the fabrication of containers for blood and related substances. In Mr. Heckman's letter to the members of the Committee, he pointed out, on Mr. Miller's instructions, that the distribution of this material would serve as a sufficient catalyst for those who were interested in the program so that they could proceed individually to contact Dr. Green directly.

Mr. Miller announced, at the day's sessions, his belief that SPI has been of immeasurable help to Dr. Green in this particular project in view of the fact that Dr. Green has informed him that he has received some very promising leads from a number of companies represented on our Committee.

Mr. Miller then asked the Secretary to attach to the Minutes of the day's session the new protocol for the "plastics evaluation program" developed by the American National Red Cross so that all interested members of the Committee may study it. (Please Note: Attached hereto as Exhibit A is the March 1, 1969 draft of the new "protocol.")

instances, it is not possible to identify a questioner or commenter. In such cases, the transcript simply indicates that the question or comment did come from the floor and was made the subject of appropriate discussion.

At the conclusion of the wide-ranging discussion reflected in the transcript, the Chairman of the Committee, Mr. Miller, asked for a vote from the floor to approve the action being taken on behalf of SPI in conjunction with the so-called Inter-Industry Committee to bring about desired changes in the Ramsey proposal. The Committee then approved the action as requested by Chairman Miller unanimously.

Report of Food Additives Petition Manual Subcommittee

The Committee was reminded that, at the last meeting, an ad hoc Subcommittee was appointed to begin preparing a Manual on Food Additive Petitions. Dr. Karl A. Hochschwender, American Hoechst Corporation, was appointed Chairman of this particular Subcommittee.

Dr. Hochschwender then delivered the following status report:

> "Those of you who were in attendance at the Committee's last meeting on November 7, 1968, will recall the discussion which centered on the desirability and feasibility of establishing a subcommittee of this Committee to undertake the drafting of what would ultimately amount to an SPI Food Additives Petition Manual. It was thought that such a Manual would be most helpful for technical, administrative and legal corporate personnel in the drafting of food additives petitions for incidental additives.
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> "At the November meeting, a resolution approving the project was adopted and a Subcommittee is now comprised of Messrs. Asam, Goodyear Tire and Rubber Company; Conley, Borg-Warner; Garceau, ICI America Inc.; McCartney, Standard Packaging Corporation; Morrison, Eastman Chemical Products, Inc.; Nesmith, U. S. Industrial Chemicals Company; Peake, E. I. du Pont de Nemours and Co., Inc.; Smith, Owens-Illinois; and Dr. Kenneth Morgareidge, Food and Drug Research Laboratories, Inc. The Subcommittee was also promised the assistance of SPI Legal Counsel.
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> "As matters developed, the Subcommittee convened its first meeting at the offices of Keller and Heckman on January 9, 1969. The meeting lasted several hours, and I think all who were there will agree that it was most fruitful in terms of laying the necessary foundation work for the proposed Manual. A first draft outline of the proposed Manual was drawn up at the meeting. The outline provided that, tentatively, the Manual shall be divided into the following seven parts:
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> "Part I - Purposes and Objectives
> "Part II - General and Background Information
> "Part III - How to Approach a Potential Indirect Food Additive Problem at the Outset

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"Part IV -- How Petitions Are Processed at FDA
"Part V - Importance of Developing Analytical Data
"Part VI - Toxicology-Protocols and Reports
"Part VII - Sample Petitions (To Be Used As Appendices to the Manual)

"Members of the Subcommittee were assigned to work on one or more of the various sections of the Manual, and it was hoped that a 'first draft' of part of the Manual could be prepared and distributed to Subcommittee members prior to this Meeting.

"Unfortunately, the actual preparation of such a first draft has been delayed partly because the press of other urgent business has prevented Counsel, and several other members of the Subcommittee from being able to complete their respective assignments; and, perhaps more importantly, because of the recent significant developments at the Food and Drug Administration (namely, the now "semi-official" FDA proposal to amend Part 121.2500 of the Food Additive Regulations) which could have great impact on the way in which the subject matter of our Manual will be presented.

"These latest developments at FDA will necessitate some further thinking and possible reevaluation of the type and extent of information that should be included in any proposed Food Additive Petitions Manual.

"We do intend to go forward with this project diligently, however, so I urge those members of the Subcommittee who have not, as yet, completed their first assignments to do so at the earliest possible time. I believe I can feel quite safe in assuring the full Committee that we shall have more tangible results to report by the time of the next meeting.

"Thank you."

Reports on Liaison with Other Organizations

Mr. Miller pointed out that, by tradition, the Committee hears at each of its meetings general reports on the interests and activities of other associati ns and groups vis a vis FDA activities.

Synthetic Organic Chemical Manufacturers Association (SOCMA)

W. P. Munro, American Cyanamid Company, delivered the following status report:

"Since the last meeting of the SPI Food, Drug and Cosmetic Packaging Materials Committee, the members of the SOCMA Dyes Additives Committee have been supplied with the text of the

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Ramsey proposal. No further action has been reported. It is believed that the liberalized features of the Ramsey proposal will not greatly affect the position of dyes as indirect food additives.

"It is suspected that Food Additives Petition 367 will be delayed further, while the Ramsey proposal is being considered."

In addition to his prepared report, Mr. Munro commented in response to a question that the long pending SOCMA petition to clear organic dyes for use with paper products remains pending and that no immediate action is anticipated despite the long delay. The general feeling of SOCMA is that the Food and Drug Administration may well await some final action on the Ramsey proposal before acting on the petition since the two subjects could have some interrelation.

Pharmaceutical Manufacturers Association - SPI Liaison Group

Chairman Miller called upon Watt Ackart, Union Carbide Corp., and Chairman of the liaison group between SPI and the Pharmaceutical Manufacturers Association, who presented the following report:

"You will recall that the joint PMA-SPI study of methodology for testing polyolefin containers for tablets, capsules, oral powders, granules and ophthalmic pharmaceutical products has been the main concern of this group since its reactivation in 1967. At the November 1968 meeting of this committee we reported that the Quality Control Section of the PMA had agreed to publish the methodology in the National Formulary but for ophthalmic products only and that opposition had developed regarding publication of the method as applied to dry products. At the last meeting we were instructed to pursue this further and expedite, if possible, the dry products publication.

"Last March, Matt Smith and I met in Detroit with representatives of the PMA and learned that the reluctance on the part of the PMA Quality Control Section was due to a feeling that the tests without numerical limits were of little value and represented only additional testing requirements which should not be encouraged. At this Detroit meeting, the concept was developed that the test procedures might be acceptable to the PMA if the resin and/or container suppliers accepted the responsibility for carrying them out. To sell this idea, the SPI was invited to send two speakers to address the spring meeting of the PMA. We made no formal commitment pending instructions from our Steering Committee.

"Last April, at a joint meeting of our Liaison Group with the Steering Committee of the SPI FD & C Packaging Materials Committee, this proposal was discussed and it was agreed that

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the PMA invitation should be declined with thanks since SPI member companies could not be committed to conducting such a testing program without discussion in the full committee. We subsequently advised the PMA of this position. It was further agreed that the whole question of the regulation of drug packaging was both unclear and unrealistic and that the SPI might well spearhead an attempt at simplification starting with polyolefin containers for dry pharmaceuticals. The PMA Liaison Group was instructed to prepare a proposal for a simplified procedure. A draft of such a procedure has been prepared and circulated for comments among members of the PMA Liaison Group. There have been no major objections which cannot be reconciled and it is hoped that a consensus draft can be prepared and circulated to this full committee either as an appendix to the minutes or as a separate mailing. We would then hope that our proposal meets with the approval of this committee and with the SPI as a whole. We expect then to approach the PMA and with their approval then to discuss our proposal with FDA in the hope that it can be incorporated into their Drug Regulations.

"Meanwhile, the methodology will appear in the National Formulary without numerical limits and applied to ophthalmic products only. Our friends in the PMA will continue to try for extension of the methodology to dry products but they are not hopeful of much success without our active support."

During the course of the day's meeting it was agreed among the members of Dr. Ackart's group that a meeting would be held in Detroit, Michigan, towards the end of July to go over the draft document prepared for ultimate presentation to the Pharmaceutical Manufacturers Association, and perhaps thereafter to the Food and Drug Administration. After the group meets in Detroit as planned, it is likely that the draft will be placed in final draft form. At this point, it will be circulated to the full Food, Drug and Cosmetic Packaging Materials Committee of the Society for comments, after which appropriate meetings will be arranged with representatives of the Pharmaceutical Manufacturers Association to discuss the SPI concept. Depending on the outcome of such sessions, further action will be taken appropriate to the circumstances and the full Committee will be kept advised of all developments.*/

*/ This group met on August 6 in Detroit and decided that rather extensive revisions to its first draft will be necessary prior to its circulation to the full Committee for review. Dr. Ackart is presently revising the material for additional consideration by the group.

Manufacturing Chemists' Association (Food Drug and Cosmetic Chemicals Committee)

Taylor W. Hanavan, E. I. du Pont de Nemours & Co., Inc., delivered the following report on activities within MCA of interest to the Committee:

"The Manufacturing Chemists' Association met on April 2, 1969. Very little was discussed of direct interest to the plastics industry. One aspect of discussion though is directly pertinent. The U. S. Food and Drug Administration did not accept the MCA request, and the requests of many others, that food chemical plants be exempt from the new Good Manufacturing Practices Regulations for food plants. Final regulations have been issued without any exception for such plants.

"There was some discussion at the MCA meeting as to what the regulations will mean to the food chemical industry, which, I think, would have equal application to the food packaging industry. It was the consensus of the people present - not, I hasten to make clear, the official consensus of the committee - that a "wait and see" attitude would be appropriate; that is, wait and see how FDA will attempt to implement the regulations in connection with the food chemical plants or food packaging operations.

"In this regard, the Food Chemical News issue of June 16, contains some fairly interesting commentary excerpted from a presentation given by Alfred Bernard, Associate Director of FDA's Bureau of Compliance, at a meeting of the Federal Bar Association on June 12. As reported in FCN:

> "Bernard said that 'FDAers on the administrative side have been uncertain for some time just to what extent the Good Manufacturing Practice Regulations have the force and effect of law.' Bernard conceded that when work started on the Good Manufacturing Practice Regulations five years ago 'they were regarded by us and by the industry generally as interpretive regulations' which 'merely expressed FDA's views as to what procedures would constitute compliance, and that there was ample latitude for industry to use other methods or techniques which might be equally or more effective in achieving compliance with the law itself.' More recently, Bernard continued, HEW Counsel William W. Goodrich 'has apprized us that these regulations have essentially the full force and effect of law.' Bernard noted disagreement with the staff by industry lawyers.
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> "The FDAer expressed doubt that FDA 'will get a court interpretation of the question as a result of direct enforcement action.' He explained: 'The problem is

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that FDA is quite unlikely to bring a legal action for violation of Good Manufacturing Practice Regulations unless the conditions are so bad that they either totally discourage vigorous defense or so surely constitute a violation of the law per se as to be independent of these regulations.'"

American Paper Institute

James R. S. McCartney, Standard Packaging Corp., reported that he had nothing more to relate on activities within the American Paper Institute than the information Mr. Heckman was covering in his report on the work of SPI in connection with the Ramsey proposal.

Can Manufacturers Institute

Charles J. Spiegl, Continental Can Co., Inc., also indicated that he had no further report to deliver at the day's meeting other than to point out that the Can Manufacturers Institute is participating in the Inter-Industry Committee dealing with FDA and that the Institute is taking no other independent action of any sort.

SPI Food and Drug Bottling Committee of the Plastic Bottle Division

M. E. Smith, Owens-Illinois, delivered the following report:

"The Food and Drug Bottling Committee is working with the Mayonnaise Salad Dressing Institute to develop test procedures and performance data for three types of dressings packaged in different plastic containers. The task group will use standard formulae for three dressings consisting of:

1. Non-separating French
2. Separating French
3. Spoonable Salad Dressing

"Two size containers, an 8 oz. and 16 oz. will be used. Approximately 2500 containers for each material will be required.

"PVC and XT resins are to be tested. The task force has decided not to work with Barex at this time since it has not yet been approved for food use by FDA. They will not test polyethylene since its gas barrier properties are so much poorer than either PVC or XT.

"The Food and Drug Bottling Committee at their next meeting on July 10th, will decide what PVC types will be used. The testing program will be run for six months at which time a final report will be written.

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"Bill Cummings of Creative Packaging Company will be the new Food Bottling Subcommittee Chairman. This Subcommittee is still working on putting together a "Primer for Food Bottling."

Report of Technical Information Subcommittee

Chairman Miller next called for a report from the Technical Information Subcommittee, to which, from time-to-time, the overall Committee refers technical problems for handling.

One of the continuing services of the Technical Information Subcommittee has been to provide at each session a listing of recently promulgated Food Additive Regulations of interest. Thus, Mr. Willard M. Westveer, The Dow Chemical Company, presented such a listing and highlighted the issued regulations which he felt of particular significance. (Please Note: Attached hereto as Exhibit C is Mr. Westveer's report on recently promulgated Food Additive Regulations.)

Status Report - Activities of SPI
Plastics Waste Disposal Committee

George W. Ingle, Monsanto Company, and Chairman of a recently formed SPI committee dealing with plastics waste disposal delivered the following status report:

"This Committee is completing its organization with emphasis so far on clarifying its mission and objectives.

"Mission is to study the problems associated with the disposal of plastics within the framework of present and future systems for solid waste management; to provide positive information to the public, and responsible leadership in implementing these solutions toward better management of our environment.

"This mission has been analyzed in terms of a series of specific objectives. These will be implemented by a limited Committee organization via two subcommittees. I - Communications (Publications and Public Relations) and II - Technical Liaison (Information Sources, and Inter-Group Liaison), additional subcommittees may later be necessary.

"Chief among the twenty odd objectives is for the Communications Subcommittee to prepare an in-depth document 'Proposals for Disposal of Plastic's Waste', by composition, product, end-use, origin, distribution by volume, in residential, municipal and industrial categories (present and future) by disposal routes new and old.

"Preparation of this document will require parallel effort by the Technical Liaison Subcommittee. This will encourage compilation from member companies, of data on identity, corrosivity, and toxicity of combustion products, distribution by volumes of all types of plastics, specific ingredients of concern (Cl, Br, Se) etc.

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"This first project for the Plastic's Waste Disposal Committee is very specific but also large and important. Volunteers from member companies will be needed to staff the two Subcommittees if this needed SPI program is to be successful.

"To identify such volunteers, and their preferred areas of activity, an organization meeting of the full Committee, and of the two Subcommittees is being scheduled for July 31.

"In the miscellaneous department:

"1) Eastman Kodak has received B. P. 1,128,793 claiming a U.V. - light disintegratable packaging material comprising a copolymer of ethylene and carbon monoxide.

"2) In a recent speech, FTC Commissioner J. M. Nicholson said 'If the price of packaging is out of proportion to the value of the product, or if the result of packaging innovation is the creation of new social problems or the aggravation of existing ones, then a more militant generation of consumers may exert massive pressures for change.'

"3) Senator Muskie's recently introduced bill (S.2005 - Resource Recovery Act of 1969) amends and extends The Solid Waste Disposal Act of 1965, aims to recover useful materials from solid waste, recommends incentives to solve SWD problems, and proposes changes in production and packaging practices to reduce solid wastes, and finally,

"4) We note an increasing number of new uses of plastics in solid waste disposal equipment.

"5) This week, New York City begins large-scale trial of polyethylene garbage bags."

Report of Lawyers' Advisory Subcommittee

Chairman Miller next called on Taylor W. Hanavan, DuPont, who presented the following report:

"At our last meeting, we noted the establishment of the National Commission on Product Safety and the fact that this organization would be conducting hearings throughout the country during the course of 1969 on household products other than foods and drugs. Since the first hearing, a hearing was held in Boston, Massachusetts, dealing with various statutory and common law legal liability problems connected with the marketing, sale and use of household products, and additional hearings have been held in

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Washington and Chicago. A series of hearings on the West Coast are now being held on various aspects of the product safety area.

"As a result of these hearings, one piece of federal legislation has been proposed - Senate Bill 1639 to amend the Federal Hazardous Substances Act to protect children from toys and other articles intended for use by children which are hazardous due to the presence of electrical, mechanical or thermal hazards.

"Another piece of federal legislation that has been introduced in the House is H.R. 6180, which would give the Commissioner of FDA authority to set up standard packaging requirements for toxic household substances. Presumably, such standards would require producers to package products designated by the Commissioner as toxic household substances in such a way as to deny access to them by children. This would be somewhat similar to the safety closure specification for aspirin bottles that FDA and industry have jointly developed. Again this bill is pending. No committee hearings have been set.

"We pointed out at the last meeting a series of bills in Congress relative to occupational health and safety. We were then talking about 1968 bills authorizing the Secretary of Labor to set up industrial hygiene safety standards for all manufacturers operating in interstate commerce. Essentially similar bills have been introduced again in this session of Congress authorizing the Secretary of Labor to set up standards and to appoint a national advisory committee to make safety standard recommendations to the Secretary.

"Actually, the bill in this area that probably will be of most interest has not yet been introduced; it will be a so-called administration bill. From what we are able to gather, the administration bill presently being contemplated would provide for a council of advisors who would be permanent federal employees responsible for the development of standards of industrial safety and recommending same to the Secretary of Labor. If the Secretary did not like a recommendation, he would have a veto power except that, if the Council of Advisors - four out of the five members as presently constituted in the proposed legislation - were to reaffirm the standard, the Secretary of Labor would have no choice but to promulgate it. The whole question of industrial safety standards is now wrapped up in a tremendous battle as to which federal agency should have complete responsibility in this area. Should it be HEW or the Department of Labor?

"We also mentioned at the previous meeting regulatory proposals by the Secretary of Labor (Willard Wirtz at that time) under

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the Walsh-Healey Act dealing with safety procedures in production facilities of federal government contractors. The procedures proposed excessively stringent safety standards in several areas. Notwithstanding protests and requested modifications, Mr. Wirtz, as one of his last contributions to the Johnson Administration, finalized his Walsh-Healey Act proposals without substantial change in the Federal Register of January 17, 1969.

"The new Administration, under Mr. Schultz, appointed a tri-partite National Safety Advisory Committee to conduct a careful review of the Regulations, at the same time postponing the effective date until May 17, 1969.

"The Advisory Committee recommended that the Secretary adopt a modified set of safety regulations which would, among other things, incorporate by reference consensus safety standards, such as those promulgated by USASI, NFPA, ASME, and ASTM, wherever possible.

"The regulations which became effective upon their publication in the Federal Register on May 20, 1969, provide for a range of permissible noise levels of from 90 decibels for an eight hour day to 115 decibels for a quarter of an hour or less.

"I might also note in passing that the regulations provide that compliance with applicable state safety, sanitary and factory inspection laws shall be deemed to be prima facie evidence of compliance with the federal regulations. However, because of the evident mandatory fashion in which government representatives are instructed to apply federal standards, any effect compliance with state laws might have is, at best, somewhat vague.

"There are two recent cases of interest I would like to mention. In deference to our sister corporation, which lost the case, I won't go into detail on the first of these - Neville Chemical v. Union Carbide, found in paragraphs 6121 of the CCH Products Liability Reports. However, I commend it to any attorney here, and suggest that non-attorneys here commend it to their attorney advisors to read. It deals with the very important issues of disclaimers of warranty, notice of limitation of claims and the time within which claims must be received.

"What I do want to discuss in some detail is the case of United States (Petitioner) v. An Article of Drug...Bacto-Unidisk...(Difco Laboratories, Inc., Claimant), 37 Law Week 4382, which I think is of considerable significance to the plastics industry in that it bears directly on an area that heretofore we all hoped might go away - that is, the area

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of surgical use of plastic products. This case involved a disc to test the sensitivity of antibiotics. I'm sure most of you are familiar with the fact that the disc itself is used as a diagnostic aid, usually by outside laboratories. The U. S. Supreme Court in a logical extension of its decision in Amp v. Gardner had little difficulty in ruling that this diagnostic aid was a 'drug.'

"A few words from the Supreme Court's opinion might illustrate the broad scope of the Court's interpretation of the meaning of the word 'drug' as defined in Section 201 (g) of the Act.

> '(T)he legislative history, read in light of the statute's remedial purpose directs us to read the classification 'drug' broadly, and to confine the device exception as nearly as is possible to the types of items Congress suggested in the debates, such as electric belts, quack diagnostic scales, and therapeutic lamps, as well as bathroom weight scales, shoulder braces, air conditioning units and crutches.... We need only point out that the (device) exception was created primarily for the purpose of avoiding the semantic incongruity of classifying as drugs (1) certain quack contraptions and (2) basic aid used in the routine operation of a hospital, items characterized more by their purely mechanical nature than by the fact that they are composed of complex chemical compounds or biological substances.'

"I think it is safe to say that with the exception of bandages, surgical swabs, sponges, sutures and possibly a few other surgically related products, industry has generally classified all surgical implant uses of plastic products as devices. The Food and Drug Administration, of course, has been attempting for a number of years to get device legislation requiring premarket approval ostensibly to go after the quack devices, 'cancer cure' products and so forth but, nevertheless, also to get statutory control over many items used for surgical applications. The Bacto-Unidisk decision now provides FDA with ample authority in the surgical use area.

"Since the Bacto-Unidisk decision, it has been reported that FDA had been in the process of developing a policy statement as to what device products the agency was now going to consider to be 'drugs.' However, we now understand that no such policy statement will be issued, at least in the near future. Regardless, it will be hard to ignore the drug implications of the Supreme Court's decision with respect to surgical implant materials.

"Assuming surgical implant materials may be classified as drugs, as plastics suppliers, consideration should be given to your company's handling of inquiries from the medical profession for

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samples of these materials. If drug use is involved, then the sample provided may be a drug component. Depending on the circumstances, and always after having checked quite carefully with your company counsel, you may then have to consider the need for special investigational drug labeling or for registering your facility as a drug production facility with the Food and Drug Administration.

"In any event, and in all cases, I strongly urge that you consult and work closely with your own company counsel on questions of this type."

Following Mr. Hanavan's report, there was a rather wide-ranging discussion among those present relative to such matters as the distinctions between drugs and devices, the regulatory ramifications of this distinction, and the precautionary steps that companies in the plastics industry should take when they supply materials to doctors, for example, for experimental work. It was strongly suggested that company officials should consult with their own counsel regarding such activities so as to avoid the possibility that, by cooperating with those in the medical profession, their companies will be subjected to unanticipated regulation by the Food and Drug Administration. Some such activity could, for example, necessitate the registering of an installation as a drug plant without any true intent or desire of management to maintain a drug plant.

International Developments

In introducing Thomas J. Hughes, Keller and Heckman, Chairman Miller said that of continuing interest to the Committee within the past several years have been developments abroad in the regulatory area.

Thomas Hughes then delivered a detailed status report on regulatory matters in the United Kingdom, the Netherlands, the activities of Codex Alimentarius Commission, and, recent contacts with other European countries. (Due to the length of Mr. Hughes' report, it is being attached hereto as Exhibit D.)

Consideration of Committee Bylaws
vis a vis New SPI Bylaws

By way of reminder, Mr. Miller noted that the SPI Board of Directors has, within recent months, developed a new "Plan for Growth" in order to assure that the Society's services to its members keep abreast with the growth of the plastics industry. In this regard, the membership of the Society overwhelmingly approved new Bylaws composed around the "Plan for Growth."

In this connection, the Steering Committee, with the help of Jerome Heckman, has reviewed the Bylaws of the SPI Food, Drug and Cosmetic Packaging Materials Committee, finding that, fortunately, there will be no need to change them in order to assure their compliance with the new Bylaws of SPI.

New Business

There was no further business offered for discussion at the day's meeting.

Next Meeting

Mr. Miller announced that, as usual, the date and site for the next meeting of the full Committee will be left up to the Steering Committee.

The day's session was adjourned at 3:00 p.m.

Respectfully submitted,

Charles L. Condit
Secretary

CLC:vw
Enclosures (4)

EXHIBIT A

THE AMERICAN NATIONAL RED CROSS

PLASTICS EVALUATION PROGRAM

PROTOCOL

MARCH 1, 1969

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SECTION 1 - INTRODUCTION

1.1 PURPOSE

The American National Red Cross (ANRC) is currently investigating new methods for the processing and preservation of blood and blood products. This research is being conducted by the ANRC Blood Research Laboratory under a contract with the National Heart Institute of the National Institutes of Health.

As a part of this program, the ANRC is conducting an evaluation of plastic materials suitable for the fabrication of blood and blood product containers to be used at temperatures from $+40^{\circ}$ to $-196^{\circ}C$. This evaluation will consist of toxicological, chemical, mechanical and clinical tests to be performed on test lots of prototype containers submitted by participating plastics and/or container manufacturers.

A basic goal of this effort is to provide a cooperative evaluation program between the ANRC and industry which will (1) identify new plastics which are potentially suitable for blood containers, (2) provide a carefully controlled comparative evaluation of these materials, and (3) provide the manufacturer with an independent set of data which may be used for license application for suitable materials. This, in turn, will serve the public interest by expediting the establishment of new improved methods of processing and preservation to insure an adequate supply of blood and blood products.

It should be noted that although this will be a comparative evaluation, it will not be competitive in the sense that any one material or container must be recommended to the exclusion of others.

1.2 PARTICIPATION

Participation in this program is open to manufacturers of plastics materials and to fabricators of plastic containers. Organizations having materials or containers which appear suitable for the uses described in Section 2.3 are invited to submit samples to the ANRC, but the ANRC reserves the right to limit the number of participants and/or materials tested. In general, only one source will be accepted for prototype containers of any given material.

1.3 DEFINITIONS

As used in this protocol or subsequent amendments thereof, the term:

(a) "American National Red Cross" or "ANRC" means the American National Red Cross, its chapters and subsidiaries, including the Blood Research Laboratory, and its subcontractors under this protocol.

(b) "Manufacturer" means an organization responsible for the production of a plastics material and/or container.

(c) "Supplier" means an organization responsible for the sale and/or distribution of a material or container.

(d) "Container(s)" means a device, including all appendages and attachments thereto, for containing blood or blood products.

(e) "Material(s)" means the polymer plastics and/or resins employed in the fabrication of the container.

(f) "Protocol" means this document and any subsequent amendments and the test procedures or other documents referenced therein.

(g) "Test Result(s)" means the data and/or interpretations thereof obtained as a result of tests performed according to this protocol.

1.4 SUBCONTRACTS

The ANRC may, as it deems necessary and with the consent of the National Heart Institute, contract other persons or organizations to perform one or more of the tests prescribed in this protocol. Except that no participating manufacturer or supplier or other organization engaged in the manufacture or fabrication of plastics materials or containers may perform such tests without prior written consent of the manufacturer(s) or supplier whose material or container is to be tested, the selection of persons or organizations to perform such tests shall be the sole responsibility of the ANRC.

SECTION 2 - PROTOTYPE CONTAINERS

2.1 ACCEPTABLE MATERIALS

The containers shall be fabricated from flexible polymeric materials (plastics) or combinations thereof. The use of pure polymeric materials, free of plasticizers, antioxidants, or other additives, is recommended. Adequate data with regard to generic name, constituents, manufacturer, and lot number shall be provided for all materials employed in fabrication of the container.

2.2 PRELIMINARY EVALUATION

Suitable samples of the candidate material(s) and data describing its general chemical and physical properties shall be submitted to the ANRC for preliminary evaluation. Evaluation of a material for prototype containers shall be based upon the data received, the results of such tests as may be deemed appropriate by the ANRC, and the opinion of the ANRC review committee, consistent with the aims and requirements of the evaluation program.

2.3 ACCEPTANCE AND CLASSIFICATION OF MATERIALS

The manufacturer or supplier of a candidate material shall be notified in writing of the decision of the review committee to accept or reject that material for further evaluation in the program. For those materials which are accepted by the committee, one or more of the following classifications will be assigned, indicating the ultimate use for which evaluation is recommended:

Class A: For storage of packed red cells, platelets and other blood products in the presence of a cryoprotective agent in the temperature range of -100 to -196°C (-148 to -365°F).

Class B: For storage of packed red cells, platelets and other blood products in the presence of a cryoprotective agent in the temperature range of 0 to -100°C (+32 to 148°F).

Class C: For collection and storage of blood and blood products in the presence of an anticoagulant solution in the temperature range of +37 to -78.5°C (+100 to -110°F).

The manufacturer or supplier may request a change in classification where additional information can be submitted to ANRC to support such a change.

2.4 TEST LOTS OF PROTOTYPE CONTAINERS

Following notification of acceptance of a candidate material for the evaluation program, the manufacturer or supplier of the candidate material shall submit to the ANRC written notice of intent to participate

in the evaluation program indicating

(a) Name of candidate material

(b) Classification (of those recommended) for which prototype containers will be submitted and solutions with which they will be filled (see Section 2.21).

(c) Name and address of manufacturer(s) or supplier responsible for submission of containers and to whom evaluation reports should be sent.

2.5 SINGLE CLASS EVALUATION

A single lot of prototype containers of each candidate material fabricated in accordance with Sections 2.10 - 2.15 of this protocol and filled in accordance with the schedules provided in Sections 2.20 - 2.22 shall be supplied to the ANRC in sealed, sterile, pyrogen-free condition except as provided in Section 2.26. The number of prototype containers required for the test lot shall be determined by the classification and appropriate schedule of solutions required.

2.6 MULTIPLE CLASS EVALUATION

For materials rated for two or more evaluation classifications, test lots will be submitted as follows:

Class AB: Submit one (1) lot as per Class A.
Class AC: Submit two (2) lots as per Classes A and C.
Class BC: Submit two (2) lots as per Classes B and C.
Class ABC: Submit two (2) lots as per Classes A and C.

2.10 CONTAINER CONSTRUCTION

The container shall consist of a main body or bag to which are attached ports, pilot tubes, and other appendages as described below. The main body of the container may be fabricated by heat or impulse sealing of flat film or extruded tubing, by molding, or by other methods consistent with the production of high quality plastic containers. The ports, pilot tubes and other appendages may be fabricated as an integral part of the main body or may be attached separately, but the use of cements or other chemical bonding agents to attach these appendages is not acceptable.

2.11 CONTAINER DIMENSIONS

The dimensions of the main body of the container, exclusive of appendages, shall be as follows:

For Class A and Class B containers:

(a) Length: 30.5 $\pm$1.3 cm (12$\pm$0.5 in.)
(b) Width: 22.9 $\pm$1.3 cm (9$\pm$0.5 in.)
(c) Wall thickness: 0.127 $\pm$ 0.051 mm (0.005 $\pm$ 0.002 in.)
(d) Internal surface area: 1290$\pm$ 130 sq.cm (200 $\pm$ 20 sq. in.)

For Class C:

(a) Length: 17.15 ± 0.64 cm (6.75 ± 0.25 in.)
(b) Width: 12.70 ± 0.64 cm (5.0 ± 0.25 in.)
(c) Wall thickness: 0.15 ± 0.076 mm (0.005 ± 0.003 in.)
(d) Internal surface area: 435 ± 20 sq.cm (67.5 ± 3.0 sq.in.)

The overall dimensions of the container, including all appendages, shall be as follows:

(a) For Class A and Class B containers - The containers, when filled according to Section 2.21, shall fit securely within a box having inside dimensions of 22.9 cm x 35.6 cm x 1 cm (9 in. x 14 in. x 3/8 in.) without undue distortion of either the box or the container.

(b) For Class C containers - The container, when filled according to Section 2.21, shall fit securely within a box having inside dimensions of 12.7 cm x 30.5 cm x 1.3 cm (5 in. x 12 in. x ½ in.) without undue distortion of either the box or the container.

2.12 CONTAINER VOLUME

The volume contained within the main body of the container shall be as follows:

For Class A and Class B containers: 675 ± 25 ml when constrained to a uniform thickness of 1 cm (0.4 in.) and a minimum of 2000 ml when unconstrained.

For Class C containers: 550 ± 50 ml.

2.13 PORTS

Each container shall have at least two (2) ports or tubes provided for filling and/or draining of the container in an aseptic manner. These ports shall be permanently attached to the edge of the bag along its width and shall extend a minimum of 2.0 cm (0.8 in.) from the edge of the main body of the container. The internal diameter of the port tube shall be such as to fit the stylet (bottle needle) of a common administration set (nominally 0.20 - 0.22 in.). Provision shall be made for a sterile hermetic closure of each port, either by heat sealing or by means of a closure device.

2.14 PILOT TUBES

Each container shall have provision for obtaining at least two (2) samples of the contents for cross-matching. These appendages shall be attached to the same edge of the bag as the ports described above. Provision shall be made for obtaining independent samples of 0.5 ml each in a sterile manner. A precalibrated pilot tube is highly desirable.

Provision for an independent tamperproof identification system for the pilot tubes and container is highly desirable to insure correct identification of blood units for cross-matching.

NOTE: The same basic device may be employed to serve as either port or pilot tube in which case a minimum of four (4) such devices shall be required.

2.15 SUSPENSION SYSTEM

Provision shall be made for securely suspending the container from hooks along either the length or width of the container as may be desired.

2.20 SOLUTIONS FOR FILLING

The following solutions will be used to fill the prototype containers according to the schedules given in Section 2.4:

(a) Anticoagulant Acid Citrate Dextrose Solution (ACD) (NIH Formula A):

Tri-sodium citrate ($Na_3C_6H_5O_7 \cdot 2H_2O$)	22.0 gm.
Citric acid ($C_6H_8O_7 \cdot H_2O$)	8.0 gm.
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	24.5 gm.
Water for injection (USP) to make	1000 ml.

(b) Anticoagulant Acid Citrate Dextrose Solution plus Adenine (AACD):

Tri-sodium citrate ($Na_3C_6H_5O_7 \cdot 2H_2O$)	22.0 gm.
Citric acid ($C_6H_8O_7 \cdot H_2O$)	8.0 gm.
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	24.5 gm.
Adenine* ($C_5H_5N_5$)	0.52 gm.
Water for injection (USP) to make	1000 ml.

(c) Anticoagulant Citrate Phosphate Dextrose Solution (CPD):

Tri-sodium citrate ($Na_3C_6H_5O_7 \cdot 2H_2O$)	26.3 gm.
Citric acid ($C_6H_8O_7 \cdot H_2O$)	3.27 gm.
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	25.5 gm.
Monobasic sodium phosphate ($Na\ H_2PO_4 \cdot H_2O$)	2.22 gm.
Water for injection (USP) to make	1000 ml.

(d) Anticoagulant Citrate Phosphate Dextrose Solution plus Adenine (ACPD):

Tri-sodium citrate ($Na_3C_6H_5O_7 \cdot 2H_2O$)	26.3 gm.
Citric acid ($C_6H_8O_7 \cdot H_2O$)	3.27 gm.
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	25.5 gm.
Monobasic sodium phosphate ($NaH_2PO_4 \cdot H_2O$)	2.22 gm.
Adenine* ($C_5H_5N_5$)	0.52 gm.
Water for injection (USP) to make	1000 ml.

(e) Glycerol Mannitol Dextrose Solution (GMD):

Glycerol ($C_3H_8O_3$)	571.0 gm.
Mannitol ($C_6H_{14}O_6$)	20.0 gm.
Sodium chloride (NaCl)	4.38 gm.
Monobasic potassium phosphate (KH_2PO_4)	1.36 gm.
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	2.75 gm.
Water for injection (USP) to make	1000. ml.

(f) Sodium chloride, isotonic (SCI):

Sodium chloride (NaCl)	9.0 gm.
Water for injection (USP) to make	1000 ml.

*NOTE: Current source of supply for adenine is from:
Dr. Grant R. Bartlett
Laboratory for Comparative Biochemistry
San Diego, California

2.21 SCHEDULE FOR FILLING

The following schedules shall be used to determine the solutions, volume of solution per container, and number of containers required for each of the designated classifications:

Container Class	Solution Code	Volume to be Filled	No. of Containers Required
A	GMD	400 ml	150
	SCI	400 ml	150
	Unfilled	-	500.
B	GMD	400 ml	100
	SCI	400 ml	100
	Unfilled	-	500
C	[illegible]	13 ml/100 ml*	100
	[illegible]D	13 ml/100 ml	100
	[illegible]	12.3 ml/100 ml	100
	[illegible]D	12.3 ml/100 ml	100
	SCI	13 ml/100 ml	100
	Unfilled	-	200

*Calculated on the nominal design volume of the container.
NOTE: For containers rated for both Class A and B use Class A.

2.22 ADDITION OR DELETION OF SOLUTIONS

The schedule for filling given in Section 2.21 may be modified by mutual agreement of the ANRC and the manufacturer(s) or supplier to permit the testing of additional solutions or to obtain a limited evaluation of a given container with a lesser number of solutions.

2.25 STERILIZATION

Where practical the container and contents shall be steam or dry-heat sterilized after filling. For those plastic materials which will not withstand steam or dry-heat sterilization, the empty container may be gas sterilized with ethylene oxide and then filled aseptically with sterile bulk solutions.

2.26 NON-STERILE CONTAINERS

Prior to sterilization a number of containers shall be removed from the test lot as follows:

5 each of those filled with ACD, AACD, CPD, ACPD, and GMD
10 each of those filled with SCI
20 each unfilled

These shall be sealed and clearly labeled "Non-Sterile". For those containers which would be sterilized with ethylene oxide, the sterile solutions will be filled into the non-sterile containers.

2.27 LABELS

A label of approximately 10 x 10 cm (4 x 4 in.) shall be affixed to one side of the main body of the container. This label shall include the following:

(a) Name and address of the primary manufacturer(s) or supplier.
(b) Lot number.
(c) Code designation of solution with which filled.
(d) Evaluation classification code, as assigned.
(e) The legend "Prototype Container for Investigational Use Only".
(f) A blank space approximately 5 x 10 cm (2 x 4 in.), for recording laboratory data.

2.28 BOXES

Each prototype container shall be enclosed in an individual plain white cardboard box of the following size:

Class A or B:
Inside dimensions: 22.9 x 35.6 x 1.0 cm (9 x 14 x 3/8 inches)
Wall thickness: 0.5 mm (0.02 in.)

Class C:
Inside dimensions: 12.7 x 30.5 x 1.3 cm (5 x 12 x ½ in.)
Wall thickness: 0.5 mm (0.02 in.)

The information required in Section 2.27 shall appear on the outside of each box, either printed directly on the box or on a label affixed to it.

2.29 ADDITIONAL CONTAINERS

Additional test lots of prototype containers may be requested by the ANRC for the purpose of further evaluation. A reasonable effort shall be made to supply these additional test lots identical in all specifications to the original test lot unless a modification of the specifications is requested by the ANRC.

2.30 TEST LOT DATA

The following information shall be supplied in writing with each test lot of prototype containers:

(a) Name and address of primary manufacturer(s) or supplier.
(b) Lot number.
(c) Trade name of material (main bag)
(d) Generic name of material.
(e) Evaluation classification code

Container

(f) List of plastic materials used for fabrication of each part of container, by part, name of material, and source.
(g) List of constituents of each plastic material, including plasticizers, antioxidants, and other additives, which are present or likely to be present in the finished container.
(h) Date(s) of fabrication

Solutions

(i) Schedule of solutions filled
(j) Source of solutions
(k) Date(s) of filling

Sterilization

(l) Method used
(m) Date of sterilization

2.31 DIVIDED RESPONSIBILITY

Where two or more establishments participate in the manufacture of the materials and the fabrication, filling and sterilization of the prototype containers, then each establishment shall be identified to the ANRC by name, address, and nature of participation.

2.32 ADDITIONAL DATA

Further information concerning the materials or containers may be requested from the manufacturer(s) or supplier when such information is deemed by the ANRC to be necessary for this evaluation. The decision to provide any or all of such information shall be at the sole discretion of the manufacturer or supplier. However, such information shall not be unreasonably withheld. The information so disclosed, unless previously published by the manufacturer or supplier, shall be considered as privileged information and shall not be disclosed by the ANRC to any other party except as provided for in this protocol or by prior written permission of the manufacturer or supplier.

2.33 LIMITED RESPONSIBILITY

Where the primary manufacturer(s) or supplier fabricates or fills prototype containers from materials of commerce or other materials not of his own manufacture, and data on these materials (e.g. constituents) is not available to him by virtue of its being proprietary or otherwise restricted, there shall be no penalty or prejudice for failure to submit this data.

2.34 DELIVERY OF TEST LOT

A reasonable period of time, mutually agreeable to the ANRC and the manufacturer or supplier, shall be allowed for the fabrication, filling, sterilization and delivery of the test lot(s) of prototype container to the ANRC.

SECTION 3 - TEST PROCEDURES

3.1 TESTS TO BE PERFORMED

Each test lot of prototype containers shall be tested to determine the suitability of the containers for use in each of the assigned evaluation classifications. Tests shall be performed for:

(a) Sterility and pyrogenicity.
(b) Toxicity
(c) Physical-chemical properties.
(d) Mechanical properties.
(e) Effects of storage at various temperatures on container materials and contents.

3.2 SAMPLING OF TEST LOTS

Upon receipt of each test lot of prototype containers, a set of consecutive serial numbers shall be assigned and affixed to the containers for purposes of sampling and recording test data. For the purpose of sampling, each subgroup consisting of all containers of a given test lot filled with a given solution or unfilled shall be considered to be separate lots. Samples shall be selected at random from these lots.

3.10 INITIAL STERILITY, PYROGENICITY AND SAFETY TESTS

Upon receipt of each test lot of prototype containers, a sample of 20 containers or 10 percent of the lot, whichever is the smaller number, shall be selected for sterility, pyrogenicity and safety tests.

3.11 UNFILLED CONTAINERS

Unfilled containers shall be tested for sterility, pyrogenicity and safety in accordance with the methods prescribed for "Transfusion and Infusion Assemblies" in U.S.P. XVII.

3.12 SODIUM CHLORIDE SOLUTION

The contents of containers filled with SCI solution shall be tested for sterility and pyrogenicity in accordance with the requirements of Section 73.73, Title 42 (PHS).

3.13 GLYCEROL-MANNITOL SOLUTION

The contents of containers filled with GMD solution shall be tested for sterility. Samples from each of these containers shall be diluted with pyrogen-free saline T.S. to a final concentration shown by previous control experiments to be non-toxic to the test animals and shall be tested for pyrogenicity.

3.14 ANTICOAGULANT SOLUTIONS

The contents of containers filled with ACD, AACD, CPD, or ACPD solutions shall be tested for sterility. Samples from each of these containers shall be diluted with pyrogen-free saline T.S. to a final concentration of 0.5 percent sodium citrate and shall be tested for pyrogenicity.

3.20 INITIAL BIOLOGICAL TESTS

Upon receipt of each test lot, a sample of 20 containers or 10 percent of the lot, whichever is the lesser number, shall be selected at random for toxicity tests (3.21), tissue culture tests (3.25) and physical-chemical analysis (3.30).

3.21 U.S.P. SPECIFICATIONS FOR TOXICITY

The containers shall be sampled and tested for toxic materials in accordance with the methods prescribed in U.S.P. XVII for Class VI plastic containers. The extractions shall be performed at 50°C for all materials and at 121°C for those containers which are sterilized by steam or dry-heat.

3.25 TISSUE CULTURE TESTS

The container materials and contents and extracts thereof shall be tested by the method of Guess, et al [J. Pharm. Sci., 54, 1545 (1965)] using mouse fibroblast cell (Strain L-929) in tissue culture.

(a) Samples of the plastic materials from various parts of the container shall be tested directly in contact with the tissue culture.

(b) The various parts of the containers shall be sampled, the samples extracted with 95% ethyl alcohol for 24 hours in a Soxhlet apparatus and the eluate evaporated to dryness. The weight of residue obtained shall be recorded. One half of the residue shall be dissolved in 95% ethyl alcohol to a final volume of 50 ml and the remainder of the residue shall be dissolved in cottonseed oil to a final volume of 50 ml. The two solutions thus obtained shall be tested for cytotoxic reactions.

(c) The contents of the filled containers shall be sampled and tested directly for cytotoxic reactions.

(d) The contents of the filled containers shall be sampled and the samples set aside for physical-chemical tests (3.30).

(e) The remainder of the contents of the filled containers shall be extracted with chloroform and the chloroform fraction tested for cytotoxic reactions.

3.30 PHYSICAL-CHEMICAL ANALYSIS

The containers obtained in Section 3.20 shall be used for physical-chemical analyses, including chemical extraction tests, infra-red (IR) and ultra-violet (UV) spectral analysis and thermogravimetric analysis (TGA).

3.31 SPECTRAL ANALYSIS OF CONTAINERS

(a) The various parts of the container shall be sampled, the samples extracted with carbon tetrachloride, and the IR and UV spectra of the extract determined using a pure solvent blank. A second set of spectra on these extracts shall be measured using the extract from a non-sterile unfilled container of the same lot as the blank.

(b) The IR and UV spectra of the ethanolic solution of the residue obtained in 3.25 (b) shall be recorded as in (a) above.

(c) A portion of the ethanolic solution of the residue obtained in 3.25 (b) shall be evaporated to dryness, the residue redissolved in carbon tetrachloride, and the IR and UV spectra recorded as in (a) above.

3.32 SPECTRAL ANALYSIS OF CONTENTS

(a) The UV spectra of the samples obtained in 3.25 (d) shall be recorded.

(b) The IR and UV spectra of the chloroform extract obtained in 3.25(e) shall be recorded.

3.33 THERMOGRAVIMETRIC ANALYSIS

The various parts of the containers shall be sampled and analyzed by TGA to establish a "fingerprint" for the material.

3.34 CHEMICAL EXTRACTION

Determination of the effects of various chemical agents on the container materials may be made, as necessary, according to the methods of ASTM D1239-55 (1965) and D543-65.

3.40 MECHANICAL TESTS

The plastic materials and containers will be tested for various mechanical properties and the effects of temperature and solutions upon these properties. Where applicable, these tests shall be conducted using standard methods of the American Society for Testing and Materials (ASTM) and in accordance with the principles established for sampling (ASTM D1898-16T), conditioning (ASTM D618-61) and low temperature testing (ASTM D759-66).

3.41 INSPECTION

Upon receipt of the test lot of prototype containers, a 5 percent sample shall be selected at random and inspected to determine that the containers and contents conform to the requirements of Section 2 of this protocol.

3.45 TESTS OF PLASTIC MATERIALS

Upon receipt of the test lot, a sample of 5 containers or 5 percent of the lot, whichever is the lesser number, shall be selected at random in accordance with Section 3.2 The various parts of the containers shall be sampled and tested as follows:

3.46 IMPACT BRITTLENESS

Samples of the material in the main body of the container will be tested according to the method of ASTM D1790-62. Tests shall be conducted at the lowest service temperature for the rated container class(A:-196°C; B:-100°C; C:-78.5°C).

3.47 TEAR RESISTANCE

Samples of the material in the main body of the container shall be tested at 23°C in accordance with the methods for initial tear resistance (ASTM D1004-66) and propagating tear resistance (ASTM D1922-67 or D1938-62T).

3.48 TENSILE STRENGTH

The tensile strength of the material in the main body of the container shall be determined at 23°C in accordance with ASTM D882-64T.

3.49 TRANSPARENCY

The transparency of the material in the main body of the container shall be determined by measurement of the absorption spectrum in the region of 350 to 700 nm. or by means of ASTM D1746-62T.

3.50 WATER ABSORPTION

The water absorption of the material in the various parts of the container shall be measured in accordance with ASTM D570-63.

3.55 TESTS ON CONTAINERS

Upon receipt of the test lot, a sample of 10 containers or 10 percent of the lot, whichever is the lesser number, shall be selected at random from each of the subgroups and tested in accordance with 3.56 - 3.60.

3.56 RUPTURE TEST

(a) Samples of the filled containers shall be placed in a non-restricting thin plastic overbag and placed on the platen of a hydraulic laboratory press. The pressure required to rupture the bag shall be recorded. Duplicate tests shall be run. If failure occurs at the closure device, the test shall be repeated using new sample containers on which the port tubes have been heat sealed close to the main body of the container.

(b) Samples of the unfilled containers shall be filled to nominal volume

(Class A or B: 675 ±25 ml; Class C : 550 ±50 ml) and tested as in part (a).

3.57 DROP IMPACT TEST

Duplicate samples of unfilled containers shall be filled with water to nominal maximum volume (Class A or B: 2000 ml; Class C: 550 ml) and tested for drop impact resistance by a modification of ASTM D2463-65T. Filled containers shall be tested as received.

3.60 ACCELERATED SERVICE TESTS

The remaining samples from each subgroup shall be subjected to ten (10) freeze-thaw cycles consisting of freezing at the lowest service temperature for the rated container class (A: -196°C, B: -100°C, C: -78.5°C) for 48 hours, thawing at +40°C and holding at room temperature (+25°C) for 24 hours before refreezing. Following the final holding period the containers shall be sampled and tested according to Sections 3.45 - 3.50.

SECTION 4 - LONG-TERM STORAGE

4.1 SAMPLING FOR STORAGE

Upon receipt of the test lot of prototype containers, samples shall be selected at random according to the following schedule:

Class A: 75 filled containers from each solution group
90 unfilled containers

Class B: 60 filled containers from each solution group
75 unfilled containers

Class C: Same as Class B.

NOTE: For containers rated for both Class A and B evaluation, use Class A schedule.

The containers shall be removed from their boxes, weighed and returned to the box. The weight and date of initial weighing shall be recorded on the label.

4.2 STORAGE TEMPERATURES

(a) Fifteen (15) containers from each solution group and 15 unfilled containers shall be placed in storage at the following temperatures:

Class A: +50, +25, +5, -85, and -170°C.
Class B: +50, +25, +5, and -85°C.
Class C: +50, +25, +5, and -25°C.

(b) Five (5) additional unfilled containers shall be placed in storage at each of the following temperatures:

Class A: +50, -85, and -170°C.
Class B: +50, -25, and -85°C.
Class C: +50, +5, and -25°C.

4.3 STORAGE PERIODS

(a) Three (3) containers from each group of the filled containers and 3 unfilled containers shall be selected at random and removed from storage at each storage temperature after each of the following intervals of storage time: 21 days, 3 months, 6 months, 12 months, and 24 months.

(b) The additional 15 unfilled containers placed in storage according to Section 4.2 (b) above shall be removed from storage after 12 months.

4.4. WEIGHT LOSS

Upon removal from storage, each container shall be allowed to attain

thermal equilibrium at room temperature for 12-24 hours. Each container shall then be removed from its box, reweighed and the new weight and weight change, if any, recorded.

4.5 TESTING OF STORED CONTAINERS

Each set of three (3) containers removed from storage shall be retested for toxicity and changes in the mechanical properties of the materials.

4.6 TOXICITY TESTS ON CONTENTS

(a) The contents of 2 containers from each set of three filled containers shall be sampled and screened for cytotoxic reactions according to Section 3.25 (c-e).

(b) If the tests in (a) are positive, the results shall be confirmed using the contents of the third container, and the spectral analysis of 3.32 performed.

(c) If (a) and (b) both yield positive tests for toxicity, then three additional containers shall be withdrawn from storage and the contents tested for sterility and pyrogenicity according to Sections 3.12 - 3.14.

4.7 TOXICITY TESTS ON CONTAINERS

(a) Samples of the plastic materials from various parts of the containers shall be tested for toxicity according to Section 3.25 (a).

(b) If the tests in (a) are positive, the containers shall be tested for toxicity in accordance with Section 3.21 and the IR and UV spectra (3.31 a) and TGA fingerprint (3.33) recorded.

4.8 MECHANICAL TESTS

(a) Samples of the materials in the main body of the containers shall be tested for impact brittleness (3.46) and transparencey (3.49) and the results compared with the results obtained initially.

(b) If significant changes are noted in (a), then the materials shall be tested by spectral analysis (3.31 a) and by TGA (3.33).

4.9 ADDITIONAL TESTS ON UNFILLED CONTAINERS

The additional unfilled containers stored according to Section 4.2 (b) shall be tested for alterations in tear resistance (3.47), tensile strength (3.48) and drop impact strength (3.57).

SECTION 5 - CLINICAL TRIALS

5.1 IN VITRO TESTS

Upon successful completion of all initial tests up to and including the 21-day storage period, the prototype containers will be tested for deleterious effects on blood and/or blood products by in vitro measurements.

5.2 PACKED RED BLOOD CELLS - CLASS A/B

(a) Five (5) sterile unfilled containers will be selected at random and filled with GMD-treated packed red blood cells (human).

(b) Two (2) sterile GMD-filled containers will be selected at random and filled with packed red blood cells (human).

(c) The filled containers will be stored for various periods of time up to 6 months at the appropriate service temperature as follows:

Class A: 7 containers at -170°C.
Class B: 7 containers at -85°C.
Class AB: 3 containers at -170°C and 4 containers at -85°C.

(d) Following storage the containers will be thawed at +40°C and the red cells deglycerolized by continuous-flow centrifugal washing according to the current methods for frozen red cells.

(e) Measurements of supernatant hemoglobin and intracellular potassium will be made throughout the above procedures and the percent recovery of red cells calculated.

5.10 ACCEPTANCE FOR CLINICAL STUDIES

Upon completion of all initial tests, in vitro tests and storage tests up to and including the 6 month period, the results of these tests will be evaluated by the ANRC Review Committee. At this time one of three (3) ratings will be assigned for each evaluation class:

1 - "Acceptable for Clinical Trials"
2 - "Continued Evaluation Recommended" - Not acceptable for clinical testing at this time. Re-evaluate in 6 months.
3 - "Not Recommended"

Prototype containers receiving a rating of "1" will be submitted for in vivo clinical trials in humans under an I.N.D. issued to the ANRC.

SECTION 6 - GENERAL CONDITIONS

6.1 MODIFICATIONS OF PROTOCOL

This protocol may be modified or amended as may be deemed necessary or desirable by the ANRC. Where feasible, notice of such amendments or modifications shall be submitted in writing to all participants prior to the effective date of change. However, the ANRC reserves the right to add, delete or alter test procedures or conditions for tests performed on any or all prototype containers or materials in a test lot and any or all test lots without prior notification.

6.2 TEST RESULTS

Results of all tests conducted under this protocol shall be submitted in writing to the Director of Research, ANRC Blood Research Laboratory or to such other personnel of this laboratory as may be designated by him.

6.3 FINAL EVALUATION

At the completion of the evaluation program or at the termination of testing of a given prototype test lot for any reason, the test results obtained to that date will be evaluated by the ANRC Review Committee and one of the following ratings assinged for each evaluation classification:

1 - "Acceptable for Use, Class __"
2 - "Acceptable for Restricted Use, Class __"
3 - "Not Acceptable - Re-Evaluation Recommended"
4 - "Not Acceptable"

6.4 REPORTS TO PARTICIPANTS

Reports of the test results obtained on each plastic material and/or prototype container shall be submitted by the ANRC to the primary manufacturer(s) or supplier of that material or container as indicated in Section 2.4. Interim reports shall be submitted at the completion of each test phase and/or storage period. A final summary report, including the evaluation and recommendations of the ANRC Review Committee shall be submitted at the end of the program or upon termination of testing of a given prototype lot for any reason.

Submission of such reports shall constitute the full responsibility or obligation of the ANRC to that manufacturer or supplier.

6.5 REPORTS TO NIH

In accordance with the terms of a contract between the ANRC and the National Heart Institute, National Institutes of Health, reports of

the test results and the interpretations and evaluations thereof shall be submitted by the ANRC to the NIH.

6.6 OTHER REPORTS

Reports of the test results, interpretations and evaluations thereof, and data and other technical information concerning the plastic materials and/or prototype containers which may be submitted to the ANRC by the manufacturer(s) or supplier shall be considered as privileged information and shall not be transmitted to any other persons except as provided for in this protocol or by prior written consent of both the ANRC and the manufacturer(s) or supplier of the plastic material and/or container in question.

6.7 NON-ENDORSEMENT OF PRODUCTS

Acceptance of a plastic material and/or prototype container for testing by the ANRC or the results of such tests shall under no circumstances be construed as an endorsement of said plastic material and/or container by the American National Red Cross or the National Institutes of Health.

6.8 TERMINATION OF TESTS

(a) Under normal circumstances, the evaluation will commence on the date of receipt of the test lot of prototype containers by the ANRC and shall continue for a period of 24 months unless terminated for other reasons.

(b) The ANRC reserves the right to discontinue testing any or all plastic materials and/or prototype containers or to terminate the evaluation program at any time. In the event such action is necessary, a written statement of intent and the reasons for such action shall be sent to the participants.

(c) The right to withdraw from this evaluation program at any time is reserved to the manufacturer(s) or supplier upon written notice of intent to the ANRC indicating the reasons for such withdrawal.

(d) Upon premature termination of the evaluation program or withdrawal by the participants, the ANRC shall, upon request, destroy or return to the manufacture(s) or supplier all existing prototype containers received therefrom.

PLASTICS EVALUATION PROGRAM

PROTOCOL

SUPPLEMENT NUMBER 1

APRIL 1, 1969

Blood Research Laboratory
9312 Old Georgetown Road
Bethesda, Maryland 20014

Effective April 1, 1969, the following amendments to the ANRC Plastics Evaluation Program Protocol of March 1, 1969 are hereby adopted, as provided for in section 6.1 of the protocol.

1. The Table of Contents is AMENDED by deletion of the following section:

   3.33 THERMOGRAVIMETRIC ANALYSIS

2. The Table of Contents is AMENDED by addition of the following sections:

   2.16 DONOR TUBE
   2.23 CONTROL SAMPLES

3. Section 2.10 is AMENDED to read as follows:

   2.10 CONTAINER CONSTRUCTION

   The container shall consist of a main body or bag to which are attached ports, pilot tubes, and other appendages as described below. The main body of the container may be fabricated by heat or impulse sealing of flat film or extruded tubing, by molding, or by other methods consistent with the production of high quality plastic containers. The ports, pilot tubes, and other appendages may be fabricated as an integral part of the main body or may be attached separately. Solvent welding or similar techniques may be employed, but the use of cements or other chemical bonding agents which are not subsequently removed or dissipated from the container is not acceptable.

4. Section 2.11 is AMENDED to read as follows:

   For Class A and Class B containers:

   (c) Nominal wall thickness: 0.076 to 0.178 mm (0.003 to 0.007 in.) with normal manufacturing tolerances.

   For Class C containers:

   (c) Nominal wall thickness: 0.076 to 0.226 mm (0.003 to 0.009 in.) with normal manufacturing tolerance.

5. Section 2.16 is ADDED as follows:

   2.16 DONOR TUBE

   Class C containers shall be provided with a length of flexible plastic tubing of approximately 91 cm (36 in.) in length for the collection of blood from the donor. This tube shall be attached to the same edge of the bag as the ports and shall have a 15 or 17 gauge needle with sterile cover attached to the distal end of the tubing.

6. Section 2.23 is ADDED as follows:

2.23 CONTROL SAMPLES

Two (2) separate samples of 25 ml each of each of the bulk solutions filled into the prototype containers shall be supplied to the ANRC in sealed glass vials or ampoules. These samples shall have been sterilized in a manner identical to that employed for the prototype containers.

7. Section 2.27 is AMENDED to read as follows:

(e) The legend "Prototype container manufactured for the American National Red Cross Plastics Evaluation Program. CAUTION: New Drug - limited by United States law to investigational use."

8. Section 3.25 is AMENDED to read as follows:

(b) Samples of the solution obtained from the extractions performed in section 3.21 for the U.S.P. tests shall be tested for cytotoxic reactions in tissue culture.

(e) The remainder of the contents of the filled containers shall be extracted with carbon tetrachloride (CCl_4) and the organic phase tested for cytotoxic reactions.

9. Section 3.30 is AMENDED by deletion of the words "and thermogravimetric analysis (TGA)".

10. Section 3.31 is AMENDED by deletion of parts (b) and (c).

11. Section 3.32 is AMENDED to read as follows:

(b) The IR and UV spectra of the carbon tetrachloride extract obtained in 3.25 (e) shall be recorded.

12. Section 3.33 is DELETED.

13. Section 3.46 is AMENDED to read as follows:

3.46 IMPACT BRITTLENESS

Samples of the material in the main body of the container will be tested according to the method of ASTM D1790-62 or by use of a calibrated air impact hammer. Tests shall be conducted at the lowest normal service temperature for the rated container class (A: -180°C; B: -85°C; C: -78.5°C). The tests will be repeated after conditioning of a second set of test samples for 48 hours at the test temperature.

14. Section 3.48 is AMENDED to read as follows:

3.48 TENSILE STRENGTH

The tensile strength of the material in the main body of the container shall be determined at 23°C in accordance with ASTM D682-64T (Method A).

15. Section 4.7 is AMENDED as follows:

(b) DELETE the words "and TGA fingerprint (3.33)".

16. Section 4.8 is AMENDED as follows:

(b) DELETE the words "and by TGA (3.33)".