



**TOGETHER**  
*for a sustainable future*

## OCCASION

This publication has been made available to the public on the occasion of the 50<sup>th</sup> anniversary of the United Nations Industrial Development Organisation.



**TOGETHER**  
*for a sustainable future*

## DISCLAIMER

This document has been produced without formal United Nations editing. The designations employed and the presentation of the material in this document do not imply the expression of any opinion whatsoever on the part of the Secretariat of the United Nations Industrial Development Organization (UNIDO) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries, or its economic system or degree of development. Designations such as “developed”, “industrialized” and “developing” are intended for statistical convenience and do not necessarily express a judgment about the stage reached by a particular country or area in the development process. Mention of firm names or commercial products does not constitute an endorsement by UNIDO.

## FAIR USE POLICY

Any part of this publication may be quoted and referenced for educational and research purposes without additional permission from UNIDO. However, those who make use of quoting and referencing this publication are requested to follow the Fair Use Policy of giving due credit to UNIDO.

## CONTACT

Please contact [publications@unido.org](mailto:publications@unido.org) for further information concerning UNIDO publications.

For more information about UNIDO, please visit us at [www.unido.org](http://www.unido.org)



19014

Distr.  
LIMITED

ID/WG.505/5(SPEC.)  
10 June 1991

United Nations Industrial Development Organization

ORIGINAL: ENGLISH

Workshop on Technological Co-operation among  
Developing Countries for the Development of  
Pharmaceutical-related Ancillary Industries

Amman, Jordan, 4-6 November 1991

20P

**USE OF PLASTIC MATERIALS IN PHARMACEUTICAL PACKAGING\***

Prepared by

Sergio Merli\*\*

\* The views expressed in this paper are the author's and do not necessarily reflect the views of the Secretariat of UNIDO. This document has not been edited.

\*\* FICETEC SpA, Milan, Italy.

V.91-25458

**TABLE OF CONTENTS**

	<u>PAGE</u>
1. THE ROLE OF PLASTICS IN PACKAGING OF PHARMACEUTICALS	1
2. TYPES OF PLASTIC MATERIALS USED IN PACKAGING OF PHARMACEUTICALS	5
3. PROPERTIES OF PLASTICS AND THEIR APPLICATIONS IN THE PHARMACEUTICAL INDUSTRY	9
4. FACTORS HAVING A BEARING ON THE CHOICE OF CORRECT PLASTIC MATERIAL	11
5. ECONOMIC AND QUALITY ASPECTS OF PLASTIC	13
6. ADVANTAGES/DISADVANTAGES OF CHOICE OF PLASTIC AS PACKAGING MATERIAL	19

1. **THE ROLE OF PLASTICS IN PACKAGING OF PHARMACEUTICALS**

THE PATH OF PACKAGING DEVELOPMENT WILL FOCUS ON PLASTICS, THEY ARE A COMMON THREAD RUNNING THROUGH THE MAJOR PACKAGING CHANGES FORECAST FOR THE NEXT DECADE.

THIS PERSPECTIVE IN PLASTIC PACKAGING DEVELOPMENTS, CAN BE RELATED TO THE IMPACT OF THE CHANGING COST OF ENERGY AND RESIN, TO THE COMPARATIVE ECONOMICS OF THE VARIOUS PACKAGING MATERIALS AND TO THE FACT THAT, IN SOME RESPECTS, THE PLASTIC PACKAGING COULD BE CHARACTERIZED AS MOVING FROM LOW TECH TO HIGH TECH.

TRENDS PARTICULARLY WILL REFLECT:

- INCREASED USE OF PLASTICS THAT DISPLACE GLASS, AND IN SOME CASES METAL CONTAINERS. GLASS PACKAGING IS THE MOST VULNERABLE PACKAGING MATERIAL AND THE METAL TUBES TOO ARE VULNERABLE, ALTHOUGH NOT TO THE EXTENT OF GLASS.
- FLEXIBLE PACKAGING WILL GROW IN ITS SOPHISTICATION AS A PACKAGING MATERIAL. THE ORIGINS OF FLEXIBLE PACKAGING DATE BACK TO ITS USE AS A BAG OR WRAP, USING COMMODITY TYPE FILMS, RELATIVELY UNSOPHISTICATED CLOSURES AND PROVIDING MINIMAL BARRIER PROTECTION. THIS HAS CLEARLY CHANGED, AND CAN BE EVIDENCED BY THE ABOVE-AVERAGE GROWTH OF BOTH MULTILAYER LAMINATIONS AND CO-EXTRUSIONS.

- REDUCED PACKAGING COST ACHIEVED THROUGH IMPROVED MATERIAL PERFORMANCE. THE NOTION THAT THE ONLY PATH TO REDUCING PACKAGING COSTS IS TO LOWER THE MATERIAL COSTS HAS LITTLE FOUNDATION.

UNLIKE MOST OTHER PRODUCTS THE PACKAGING MUST PERFORM A VARIETY OF ROLES - WITHIN THE PACKAGING AND FILLING LINE, IN STORAGE, IN TRANSPORTATION AND, FINALLY, AS A FUNCTIONAL VEHICLE FOR THE USE OF THE PRODUCT.

WHEN ONE CONSIDERS ALL OF THE ROLES THAT THE PACKAGE MUST PLAY, IT BECOMES INCREASINGLY EVIDENT THAT IMPROVED PERFORMANCE OUTWEIGHS THE SIMPLE NEED OF LOWER COSTS.

- PACKAGING WILL CONTINUE TO GET LIGHTER. THE IMPLICATIONS OF THIS DEVELOPMENT EXTEND INTO MANY DIRECTIONS.

FOR INSTANCE, THE SUBSTITUTION OF LIGHTER WEIGHT FLEXIBLE PACKAGING AND PLASTIC CONTAINERS/JARS FOR METAL AND GLASS, WILL SHARPLY REDUCE THE COST OF TRANSPORTATION FOR MANY OF THESE PRODUCTS, THROUGH A LIGHTER PALLET LOADS FOR THE SAME CUBIC SPACE, WHICH, FURTHERMORE, SHOULD LESSEN DEMANDS UPON TRAILERS AND FORK-LIFT TRUCKS.

FOR THE MOST PART, THE PACKAGING TRENDS THAT ARE PROJECTED TO OCCUR DURING THE NEXT FUTURE SHOULD BE OF NO SURPRISE TO THE PACKAGING COMMUNITY.

PACKAGING CHANGE TENDS TO BE EVOLUTIONARY, RATHER THAN REVOLUTIONARY. IT WOULD APPEAR THAT ONCE THE CONSUMER HAS ACCEPTED A PACKAGE AS A STANDARD WITHIN A CATEGORY OF PRODUCTS, ITS HABITUAL USE MAY CREATE AN INVISIBLE BARRIER THAT IS OFTEN QUITE DIFFICULT TO CHANGE. BUT THERE ARE OTHER CONSIDERATIONS WHICH CAUSE PACKAGING CHANGE TO BE EVOLUTIONARY. SOME OF THE MORE IMPORTANT INCLUDE: THE INVESTMENT IN PACKAGE HANDLING AND FILLING MACHINERY; GOVERNMENT STANDARDS AND REGULATIONS, AND THE METHOD OF STORAGE REQUIRED FOR A PRODUCT.

THE STEADY INCREASE OF THE AVAILABLE TYPES OF PLASTICS ALLOWS INNOVATIONS IN PACKAGING DESIGN, WITH FUNCTIONAL, AESTHETICAL AND ECONOMIC BENEFITS (NOT ALWAYS OBTAINABLE WITH THE TRADITIONAL MATERIALS) FOR THE MANUFACTURERS, DISTRIBUTORS AND THE END USERS.

THE CARDINAL RULE IN PACKAGING IS TO PRESERVE THE PRODUCT, AND THIS IS ALL THE MORE TRUE WHEN THE PRODUCT TO BE PACKAGED IS A PHARMACEUTICAL ONE.

WE KNOW VERY WELL THAT A GREAT DEAL OF PHARMACEUTICAL PRODUCTS ARE ABLE TO FAILURE, IF THEY ARE NOT SUITABLY AND PROPERLY "PROTECTED" DURING THE SHELF-LIFE TIME. HENCE IT FOLLOWS THAT THE CHOICE OF THE PACKING PLASTIC MATERIAL PLAYS THE LEADING ROLE.

THE PLASTIC MATERIALS, UTILISED IN THE PACKAGING OF THE PHARMACEUTICAL PRODUCTS, CAN BE SUMMARIZED IN THE FOLLOWING POLYMER FAMILIES:

- POLYETHYLENE
- POLYPROPYLENE
- POLYSTYRENE
- POLIVINYL CHLORIDE
- POLYVINYLIDENE CHLORIDE (SARAN)
- POLYCARBONATE
- EVOH COPOLIMER
- POLYESTER (PET)
- POLYFLUOROCARBON
- IONOMER RESINS

IN SHORT, THE CHARACTERISTICS OF THE MAIN POLYMER FAMILIES ARE MENTIONED.

## 2. TYPES OF PLASTIC MATERIALS USED IN PACKAGING OF PHARMACEUTICALS

### POLYETHYLENE

THE POLYETHYLENE FAMILY INCLUDES THE LOW-DENSITY POLYETHYLENE (LDPE), THE LINEAR LOW-DENSITY POLYETHYLENE (LLDPE) AND THE HIGH-DENSITY POLYETHYLENE (HDPE).

AS FAR AS THE CHEMICAL PROPERTIES ARE CONCERNED, THE WATER VAPOR TRANSFER RATE (WVTR) OF LDPE IS 1.2, OF LLDPE IS 1.2, OF HDPE IS 0.3 TO 0.65, AND THE GAS TRANSMISSION RATE (REFERRED TO O<sub>2</sub>) OF LDPE IS 250 TO 840, OF LLDPE IS 250 TO 840, OF HDPE IS 33 TO 250.

LLDPE AND HDPE RESINS HAVE PHYSICAL PROPERTIES WHICH ARE SUPERIOR TO THOSE OF CONVENTIONAL LDPE.

### POLYPROPYLENE

THE POLYPROPYLENE FAMILY INCLUDES THE ORIENTED POLYPROPYLENE (OPP) AND THE NON-ORIENTED POLYPROPYLENE (NOPP).

AS FAR AS THE CHEMICAL PROPERTIES ARE CONCERNED THE WVTR OF OPP IS 0.3 TO 0.4, OF NOPP IS 0.5 TO 0.65, AND THE GAS TRANSMISSION RATE OF OPP IS 110, OF NOPP IS 84 TO 415.

BOTH THE RESINS HAVE GOOD PHYSICAL PROPERTIES.



POLYVINYL CHLORIDE

THE POLYVINYL CHLORIDE (PVC) CONTINUES TO BE ONE OF THE MOST VERSATILE PACKAGING MATERIALS AND THE VERY FACT THAT PVC'S PROPERTIES CAN BE TAILORED SO SPECIFICALLY ENABLES PVC TO OCCUPY A BROAD MARKET SPECTRUM.

THE WVTR OF THE PVC IS ABOVE 4 AND THE GAS TRANSMISSION RATE IS 5 TO 1500. DUE TO THE RELATIVELY HIGH WVTR THAT DOES NOT ALLOW IN MANY CASES THE USE OF THE PVC ALONE IN THE PHARMACEUTICAL PACKAGING, THE PVC IS CO-EXTRUDED IN ORDER TO PRODUCE A COMPOSITE STRUCTURE OF SEVERAL PLASTIC MATERIALS WHICH HAS THE ABILITY TO PROTECT PRODUCTS FROM MOISTURE AND OXYGEN.

POLYVINYLIDENE CHLORIDE

THE POLYVINYLIDENE CHLORIDE IS MADE FROM A COPOLYMER THAT IS PREDOMINANTLY VINYLIDENE CHLORIDE (PVDC). DUE TO THE VERY HIGH CHLORINE CONTENT OF THE POLYMER, PVDC HAS AN EXTREMELY HIGH BARRIER TO PASSAGE OF OXIGEN AND WATER VAPOR. IN FACT THE WVTR IS 0.05 TO 0.3 AND THE GAS TRANSMISSION RATE IS 0.08 TO 1.7.

POLYCARBONATE

POLYCARBONATE IS ONE OF THE STRONGEST AND MOST RIGID THERMOPLASTICS. THESE PROPERTIES ARE MAINTAINED OVER A WIDE RANGE OF TEMPERATURES AND LOADING RATES.

POLYCARBONATE FILM MEETS MANY REQUIREMENTS OF MEDICAL PACKAGING, IN WHICH THE WATER VAPOR IS NOT A CRITICAL FACTOR: IMPERMEABILITY TO BACTERIA, COMPATIBILITY WITH STANDARD STERILIZATION METHODS (AUTOCLAVE, GAMMA RAYS, ETHYLENE OXIDE), A LONG SHELF LIFE AND DURABILITY.

THE WVTR OF POLYCARBONATE IS 9.7 AND THE GAS TRANSMISSION RATE IS 258.

POLYETHYLENTEREPHTHALATE

THE POLYETHYLENTEREPHTHALATE (PET), BECAUSE OF ITS THERMAL PROPERTIES WITH A NORMAL TEMPERATURE RANGE FOR PROLONGED USE OF -70° TO 150°C, CAN BE PROCESSED AND USED IN APPLICATIONS OVER A WIDER TEMPERATURE RANGE THAN MOST COMMON PACKAGING FILMS.

THE WVTR OF PET IS 1.3 AND THE GAS TRANSMISSION RATE IS 5. PET FILMS CAN BE USED IN STEAM, ETHYLENE OXIDE AND RADIATION STERILIZATION PROCESSES.

ETHYLENE VINYL ALCOHOL

THE OUTSTANDING CHARACTERISTICS OF ETHYLENE VINYL ALCOHOL RESINS (EVOH) IS THEIR ABILITY TO PROVIDE A BARRIER TO GASES (THE GAS TRANSMISSION RATE IS 0.05 TO 0.18) AND TO WATER VAPOR (THE WVTR IS 1.4 TO 5.4).

EVOH IS ONE OF THE ONLY THREE TYPES OF POLYMERS THAT MEETS THE GENERALLY ACCEPTED DEFINITION FOR "HIGH BARRIER POLYMER".

COMBINATIONS OF EVOH WITH LESS EXPENSIVE POLYMERS, SUCH AS POLYETHYLENE, POLYPROPYLENE AND OTHERS OFFER AN ECONOMICAL HIGH PERFORMANCE PACKAGING MEDIUM.

THE ADVANCE OF PLASTICS INTO PACKAGING STEMS IN LARGE PART FROM THE VARIETY OF RESINS AVAILABLE AND THE MANY WAYS IN WHICH THEY CAN BE FORMED AND FABRICATED. RESINS CAN BE CONVERTED INTO FILMS, SHEET PACKAGES AND MANY KINDS OF RIGID FORMS.

TO A GREATER EXTENT THAN IS POSSIBLE WITH OTHER MATERIALS, PLASTICS HAVE POTENTIAL FOR BEING PROCESSED INTO CONTAINERS IN THE PACKAGER'S PLANT.

BUT AT THIS POINT, IT MUST BE STRESSED THE FACT THAT THE EXACT CHOICE OF A PLASTIC MATERIAL REQUIRES SPECIFIC KNOWLEDGE OF THE PRODUCT TO BE PACKAGED AND WHAT REQUIREMENTS WILL BE NECESSARY.

3. PROPERTIES OF PLASTICS AND THEIR APPLICATIONS  
IN THE PHARMACEUTICAL INDUSTRY

IMPORTANT FILM PROPERTIES TO BE TAKEN INTO  
CONSIDERATION INCLUDE:

- PERMEABILITY WITH RESPECT TO THE WATER VAPOR, TO  
OXIGEN, TO ORGANIC VAPORS AND TO OTHER GASES;
- LIGHT TRANSMITTANCE, IN THE VISIBLE AND IN THE  
NEAR UV;
- MONOMERS AND VOLATILE RESIDUES;
- STABILITY AND THERMIC RESISTANCE;
- HEAT SEALING, WITH RESPECT TO THE DEGREE OF  
CRISTALLINITY OF THE POLYMER AND TO DENSITY (LOW  
AND HIGH DENSITY);
- TENSILE STRENGTH;
- CHLORINATION;
- IMPACT STRENGTH;
- TEAR STRENGTH;
- PRINTABILITY AND MACHINEABILITY.

THESE PROPERTIES MUST BE EVALUATED, AS IN THE  
PHARMACEUTICAL INDUSTRY THE USE OF PLASTIC PACKAGING  
COVERS A WIDE RANGE OF APPLICATIONS:

- BLISTERS FOR THE SOLID PHARMACEUTICAL DOSAGE  
FORMS, I.E. TABLETS, FILM- AND/OR SUGAR-COATED  
TABLETS, HARD GELATIN CAPSULES;

- SACHETS, WITH THE COMBINATION OF PLASTIC MATERIALS WITH OTHER MATERIALS, SUCH AS ALUMINIUM FOIL AND/OR PAPER;
- BAGS, FOR THE IV INFUSIONS AND BLOOD DERIVATIVES;
- SOFT BOTTLES, FOR THE IV INFUSIONS;
- CONTAINERS FOR SUPPOSITORIES;
- TUBES FOR OINTMENTS;
- SMALL CONTAINERS FOR UNIT DOSE ORAL SOLUTIONS;
- SMALL CONTAINERS FOR UNIT DOSE EYE LOTIONS;
- CONTAINERS FOR AMPOULES AND VIALS.

ALL OF US ARE WELL AWARE THAT THE ESTABLISHMENT OF A PRODUCT'S SHELF LIFE FOR A SPECIFIC PRODUCT/PACKAGE/ENVIRONMENT IS VITAL TO THE PHARMACEUTICAL INDUSTRY.

THE MAJOR TECHNIQUES BY WHICH THIS CAN BE ACCOMPLISHED ARE KNOWN; ACTUAL SHELF-LIFE TESTING OR ESTIMATION, AND THE ESTIMATION TECHNIQUES BEING UTILIZED ARE ACCELERATED STORAGE TESTS AND/OR SIMULATION MODELING.

**4. FACTORS HAVING A BEARING ON THE CHOICE OF CORRECT PLASTIC MATERIALS**

IN ORDER TO REACH THE BEST RESULTS, MANY PRECISELY CORRELATED FACTORS MUST BE TAKEN INTO CONSIDERATION, BOTH FOR THE PRODUCT AND THE PLASTIC MATERIAL:

- THE COMPATIBILITY BETWEEN THE PHARMACEUTICAL ACTIVE RAW MATERIAL AND THE PLASTIC MATERIAL;
- THE KNOWLEDGE OF THE PHARMACEUTICAL PRODUCT'S CRITICAL MOISTURE LEVEL;
- THE PACKAGE PERMEABILITY WITH RESPECT TO THE WATER VAPOR;
- THE PRODUCT'S MOISTURE EQUILIBRIUM ISOTHERM;
- THE ENVIRONMENTAL DATA;
- THE HEAT SEALING OF THE PLASTIC MATERIAL;
- THE PROOFNESS TO THE MOULDS AND BACTERIA.

AS SLIGHT DIFFERENCES IN PRODUCT COMPOSITION, CRYSTAL STRUCTURE AND MORPHOLOGY CAN LEAD TO VARYING FAILURE MECHANISMS (FOR INSTANCE THE RATE OR THE SPEED OF THE DEGRADATION REACTIONS), AS VARIABILITY IN PACKAGE PROPERTIES CAN ALSO LEAD TO MARKED DIFFERENCES IN FAILURE OF THE SAME PRODUCT.

ANOTHER FACT TO THINK OF, RESULTS FROM WHAT SAID BEFORE. WHEN IT IS DECIDED TO BUY A PACKAGING MACHINERY, THE MACHINE PURCHASER NEEDS TO UNDERSTAND THAT HE IS NOT JUST BUYING A MACHINE. HE IS INVESTING IN A PACKAGING SYSTEM.

THE SYSTEM INCLUDES THE MACHINE, BUT IT ALSO INCLUDES THE PRODUCT AND THE PACKAGING MATERIAL. IN FACT, THE PRODUCT AND PACKAGE MUST BE CONSIDERED INTEGRAL PARTS OF THE MACHINE.

WHEN VIEWED IN THIS MANNER, IT SHOULD BE EASY TO UNDERSTAND THAT THE COOPERATION WITH THE SUPPLIER OF THE PACKAGING MATERIAL IS CRITICAL IN ORDER TO ACHIEVE THE RIGHT CHOICE OF THE PLASTIC PACKAGING MATERIAL (IT MUST COMPLY WITH THE SAFEGUARD OF THE PHARMACEUTICAL PRODUCT), TO GIVE TO THE MACHINE BUILDER THE CHARACTERISTICS AND THE PROPERTIES OF THE PLASTIC MATERIAL AND TO DETERMINE THE MACHINEABILITY. IN THE CHOICE OF THE PLASTIC PACKAGING MATERIAL, THE ECONOMICAL POINT OF VIEW, OF COURSE, MUST BE TAKEN INTO CONSIDERATION. A SUITABLE PROTECTION OF THE PRODUCT TOGETHER WITH A GOOD MACHINE OUTPUT AT A PRICE ACCEPTABLE EITHER BY THE MANUFACTURER AND BY THE END USER IS THE MAIN POINT TO BE CONSIDERED TO OBTAIN A SUCCESSFUL PACKAGING.

5. ECONOMIC AND QUALITY ASPECTS OF PLASTIC

THE ECONOMICAL POINT OF VIEW MUST NOT BE LIMITED ONLY TO THE CHOICE OF THE PLASTIC MATERIALS SUITABLE FOR THE PACKAGE, BUT IT IS NECESSARY TO COMPARE THE PLASTIC MATERIAL PACKAGE WITH ANOTHER TYPE OF PACKAGING. ON THIS SUBJECT, IT CAN BE CITED THE TABLETS PACKAGING AS A CLASSICAL EXAMPLE: IF THE AMOUNT OF TABLETS TO BE PACKAGED INTO THE PACKAGING UNIT IS LESS THAN 40 THE BLISTER PACKAGING IS THE RIGHT CHOICE, IN THE OTHER CASES THE PACKAGING IN BOTTLES IS MORE PROFITABLE, UNDER THE SAME CONDITIONS OF QUALITY.

QUALITY CANNOT BE SET ASIDE FROM THE PHARMACEUTICAL INDUSTRY, AND THE QUALITY HAS A HIGH PRICE. IN THIS CONNECTION THE MATERIALS SUPPLIER PLAYS AN IMPORTANT ROLE, FOR OBVIOUS REASONS.

IN ORDER TO LESSEN THE COSTS, THE TREND OF THE MODERN INDUSTRY IS TO ELIMINATE THE CONTROLS WHICH DON'T BRING IN ADDED VALUE TO THE PRODUCT, FOR EXAMPLE THE CONTROL BY SAMPLING.

SUCH BEING THE CASE, IT IS NECESSARY TO ESTABLISH A NEW SUPPLIER-CLIENT RELATIONSHIP, THAT CAN BE DEFINED THE VALIDATION OF THE SUPPLIER.



VALIDATION MEANS TO INCREASE THE KNOWLEDGE AS A WHOLE OF THE SUPPLIER, I.E. ITS RELIABILITY, ITS PRODUCTION OUTPUT, ITS PRODUCTION QUALITY.

IN ORDER TO REACH THIS GOAL, THE ITALIAN ASSOCIATION FOR QUALITY CONTROL SUGGESTS THIS TYPE OF ACTIONS:

- TO UTILIZE A QUESTIONNAIRE WHICH, ON THE PATTERN OF THE CGMP, COVERS ITEMS SUCH AS ORGANISATION, PERSONNEL, BUILDINGS, EQUIPMENT, PRODUCTION SHEETS, PACKAGING, SHIPPING AND QUALITY CONTROL PROCEDURES;
- TO DO A FIRST CLASSIFICATION OF THE SUPPLIERS;
- THE CLIENT MUST BECOME AVAILABLE TO HELP THE SUPPLIER TO IMPROVE, IF SUCH IS THE CASE;
- THE CLIENT MUST REVISE ITS TECHNICAL SPECIFICATIONS IN ORDER TO LOOSEN, IF IT IS POSSIBLE TO DO IT, THE TOO MUCH STRICT CONSTRAINTS;
- THE SUPPLIER MUST SCHEDULE A QUALITY SYSTEM, TO STANDARDIZE THE CONTROLS AND TO DO CORRECTIVE ACTIONS IN CONSEQUENCE OF FOUND DEFECTS;
- THE CLIENT AND THE SUPPLIER MUST ARRANGE RECIPROCAL VISITS TO CONSIDER PERIODICALLY THE QUALITATIVE SITUATION AND/OR TO DISCUSS SPECIFIC PROBLEMS.

WHEN BOTH THE PARTIES HAVE COME TO AN AGREEMENT UPON THE ABOVE INDICATED ACTIONS, THERE WILL BE A FIRST PHASE IN WHICH THE BATCHES OF THE MATERIALS ARE CHECKED AT THE SUPPLIER BY PERSONNEL OF BOTH THE PARTIES, ON THE GROUND OF CONTROL SCHEMES OF THE CLIENT, PREVIOUSLY AGREED. AS A FOLLOWING PHASE THE BATCHES ARE CHECKED AT THE SUPPLIER ONLY BY ITS PERSONNEL AND THE ANALYSIS DATA SENT TO THE CLIENT, TOGETHER WITH THE BATCH.

THIS SUGGESTED PROCEDURE CAN BE VERY HELPFUL BOTH FOR THE CLIENT AND THE SUPPLIER.

FOR PHARMACEUTICAL MANUFACTURERS PROPOSING TO USE PLASTIC CONTAINERS FOR THEIR PREPARATIONS A PRIMARY REQUIREMENT IS A KNOWLEDGE, OBTAINED FROM THE SUPPLIER OF THE RAW MATERIALS, OF THE COMPOSITION OF THE PLASTIC SO THAT THE POTENTIAL HAZARDS CAN BE ASSESSED. IN THIS RESPECT, TYPE SPECIFICATIONS FOR A NUMBER OF PLASTICS USED IN THE MANUFACTURE OF PLASTIC CONTAINERS FOR PHARMACEUTICALS AND THE RELATED TESTS ARE PROVIDED IN THE MOST ACCREDITED PHARMACOPOEIAS, SUCH AS USP (TWENTY-SECOND REVISION), BRITISH PHARMACOPOEIA (EFFECTIVE DATE EDITION DECEMBER 1988) AND EUROPEAN PHARMACOPOEIA (SECOND EDITION 1990).

IN USP XXII DIRECTIONS ARE GIVEN TO DETERMINE PHYSICAL AND CHEMICAL PROPERTIES OF PLASTICS AND THEIR EXTRACTS, WITH TESTS DESCRIPTION AND REQUIREMENTS TO BE MET.

IN-VITRO AND IN-VIVO BIOLOGICAL REACTIVITY TESTS ARE INDICATED, AND ON THE BASIS OF RESPONSE TO THE BIOLOGICAL TEST PROCEDURES SIX GENERAL CLASSES OF PLASTICS ARE DEFINED.

TWO SECTIONS ARE SET APART FOR PLASTIC CONTAINERS FOR OPHTHALMICS AND HIGH-DENSITY AND LOW-DENSITY POLYETHYLENE CONTAINERS.

IN B.PH. 88 REFERENCES ARE MADE TO THE EUROPEAN PHARMACOPOEIA, SOME GENERAL CHEMICAL TESTS ARE DESCRIBED AND SPECIFIC SECTIONS ARE DEDICATED TO THE STERILE PLASTIC CONTAINERS FOR HUMAN BLOOD AND BLOOD COMPONENTS, TO THE EMPTY STERILE CONTAINERS OF PLASTICISED POLY (VINYL CHLORIDE) FOR HUMAN BLOOD COMPONENTS, AND TO THE STERILE CONTAINERS OF PLASTICIZED POLY (VINYL CHLORIDE) CONTAINING AN ANTICOAGULANT SOLUTION.

IN EUROPEAN PHARMACOPOEIA [SECOND EDITION - FOURTEENTH FASCICULE - (EUROPEAN TREATY SERIES NO. 50) - 1990] PHYSICAL AND CHEMICAL TESTS, AND RELATED PROCEDURES ARE DESCRIBED, TOGETHER WITH THE REQUIREMENT TO BE MET, FOR THE FOLLOWING PLASTIC MATERIALS:

- MATERIALS BASED ON PLASTICISED POLY (VINYL CHLORIDE) FOR CONTAINERS FOR HUMAN BLOOD AND BLOOD COMPONENTS, AND FOR CONTAINERS FOR AQUEOUS SOLUTIONS FOR INTRA-VENOUS INFUSION;
- MATERIALS BASED ON PLASTICISED POLY (VINYL CHLORIDE) FOR TUBING USED IN SETS FOR TRANSFUSION OF BLOOD AND BLOOD COMPONENTS;
- POLYETHYLENE - LOW DENSITY FOR CONTAINERS FOR PREPARATIONS FOR PARENTERAL USE AND FOR OPHTHALMIC PREPARATIONS;
- POLYETHYLENE - HIGH DENSITY FOR CONTAINERS FOR PREPARATIONS FOR PARENTERAL USE;
- POLYPROPYLENE FOR CONTAINERS FOR PREPARATIONS FOR PARENTERAL USE.

AS IT CAN BE SEEN, A PARTICULAR EMPHASIS IS PLACED ON PLASTIC MATERIALS FOR CONTAINERS FOR SOLUTIONS FOR INJECTION.

WHEN SOLUTIONS FOR INJECTIONS ARE SUPPLIED IN PLASTIC CONTAINERS, STRICT CARE SHOULD BE TAKEN TO ENSURE THAT CONSTITUENTS OF THE PLASTIC ARE BOTH INNOCUOUS AND COMPATIBLE WITH PREPARATION. OBVIOUSLY THE SAME DEGREE OF CARE SHOULD BE TAKEN FOR THE PLASTIC MATERIALS PROPOSED FOR THE COMPOSITION OF THE CONTAINER FOR PREPARATIONS THAT ARE TO BE APPLIED EXTERNALLY AND/OR TOPICALLY.

IT MUST HOWEVER BE POINTED OUT THAT THE APPLICABLE REGULATIONS AS ISSUED BY THE MINISTRIES OF HEALTH OF VARIOUS COUNTRIES WITH REGARD TO THE TESTING OF PHARMACEUTICAL PACKAGING MUST BE TAKEN INTO CONSIDERATION.

A COMPARISON WITH THE CONVENTIONAL PACKAGING, SHOWS THE ADVANTAGES AND THE DISADVANTAGES OF THE PLASTIC MATERIAL PACKAGING.

6. **ADVANTAGES/DISADVANTAGES OF CHOICE OF PLASTIC AS PACKAGING MATERIAL**

**ADVANTAGES**

- LESS SPACE IN THE STORAGE OF PACKAGING MATERIALS
- LESS WEIGHT TO HANDLE
- LIGHT WEIGHT OF THE UNIT PACKAGE
- SHATTER RESISTANCE
- REDUCED BREAKAGE
- EASY HANDLING FOR THE END USER
- LOWER FREIGHT COSTS
- IN-LINE THERMOFORM, FILL, SEAL CONCEPT. TO A GREATER EXTENT THAN IS POSSIBLE WITH OTHER MATERIALS, PLASTICS ARE PROCESSED OR HAVE POTENTIAL FOR BEING PROCESSED INTO CONTAINERS IN THE PACKAGER'S PLANT
- LESS NOISE ON THE PACKING LINE
- BETTER ANSWER IN THE USE OF TAMPER-EVIDENT PACKAGING AND CHILD-PROOF PACKAGING
- MORE RESISTENT AT LOW TEMPERATURES
- LOW ENERGY USAGE
- HIGHER VERSATILITY

DISADVANTAGES

- SOME PERMEABILITY TO MOISTURE AND GASES
- MANY POLYMERS ARE TRANSLUCENT RATHER THAN TRANSPARENT
- USE OF PLASTICS CAN BE LIMITED BY THEIR TENDENCY TO TAKE UP LIPOPHILIC SUBSTANCES FROM PHARMACEUTICAL PREPARATIONS.  
A CONTAINER MADE OF THIN PLASTIC NOT ONLY ABSORBS LIPOPHILIC SUBSTANCES BUT IF THEY ARE VOLATILE, ALLOWS THEM ESCAPE
- SOME PLASTICS CAN RELEASE MONOMERS.

IN CONCLUSION IT MAY BE SAID THAT THE TREND OF THE FUTURE IS THE WIDENING OF THE USE OF PLASTIC MATERIALS, AND IN PARTICULAR OF SOME PLASTIC MATERIALS FOR OTHER PHARMACEUTICAL DOSAGE FORMS, FOR INSTANCE THE UNDERGOING TESTS OF PET BOTTLES FOR SYRUPS AND DRY SYRUPS AND THE SUGGESTED TRANSITION FROM GLASS AMPOULES TO PLASTIC AMPOULES FOR SMALL VOLUME PARENTERALS, TAKING ADVANTAGE OF THE VERY LATEST DEVELOPMENTS IN PLASTIC TECHNOLOGY. IN THE CASE OF THE AMPOULES, THE MAIN CONCERN STRESSED IS THE PARTICULATE MATTER CONTAMINATION AND HOW TO MINIMIZE IT, IN RELATION TO HEALTH RISKS.