Role of packaging material on Pharmaceutical product stability

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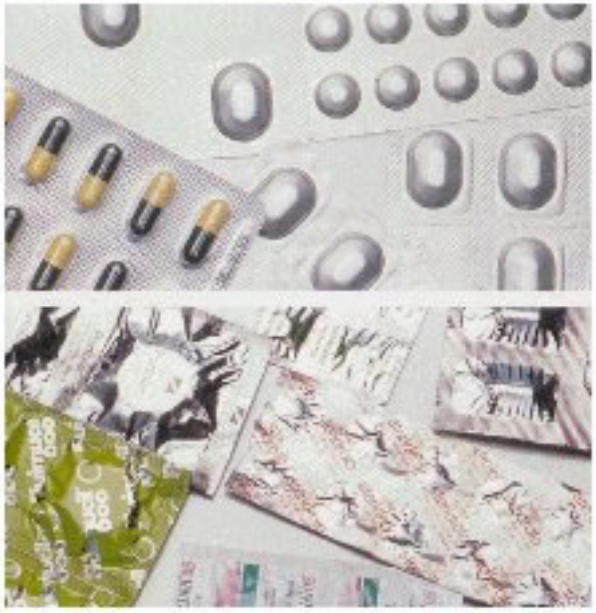
Agenda

- **General Overview**
  - **What is packaging?**
  - **Importance of packaging**
  - **Functions of packaging**
  - **Material characteristics**
- **Choosing the Appropriate Primary Pack**
  - **Suitable polymer / Blister Packs**
  - **Containers & Closures**
- **Testing of materials**
  - **QC test**
  - **QC Plus**
  - **Pack integrity**
- **Regulatory**
  - **US, EU, Pharmacopoeial**
- **Case studies**



What is packaging ?

Packaging is defined as the collection of different components which surround the pharmaceutical product from the time of production until its use.





Importance of packaging

- Protect against all adverse external influences that can alter the properties of the product.
- Protect against biological contamination.
- Protect against physical damage.
- Carry the correct information and identification of the product.
- Tamper evident / Child resistance / Anti counterfeiting.

Functions of packaging

- **Containment**
  - Not to leak, nor allow diffusion and permeation
  - Strong enough to hold the contents during handling

- **Protection**
  - Light
  - Moisture
  - Oxygen
  - Biological contamination
  - Mechanical damage
  - Counterfeiting

Material characteristics

Additional qualities required

- It must preserve the physical properties of all dosage
- forms and protect them against damage or breakage.
- It must not alter the identity of the product.
- It must preserve the characteristics properties of the
- product to comply specifications.
- It must protect product against undesirable or
- adulterating chemical, biological or physical entities.

Choosing appropriate primary pack

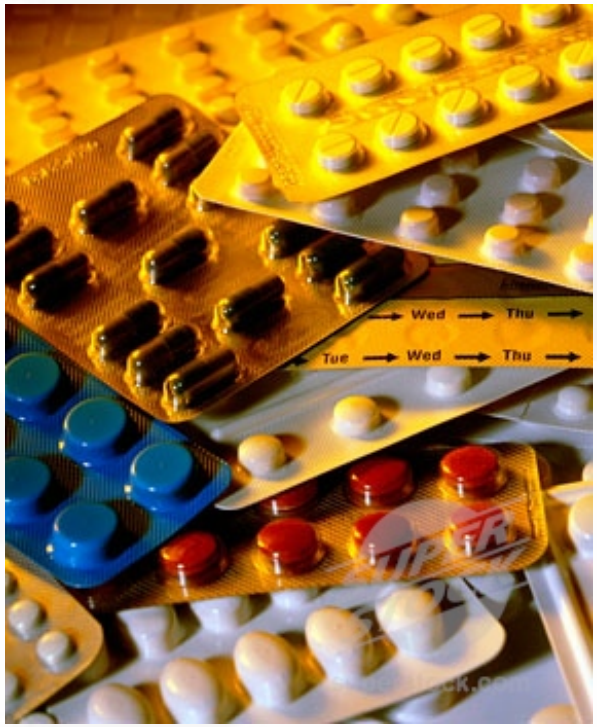
Product characteristics / sensitivity

- Hygroscopicity
- Physical degradation
- Chemical degradation
- Drug release properties
- Mechanical properties
- Photosensitivity
- Gas liberation tendency
- Dimensional aspects

Choosing appropriate primary pack

Selection of packaging material

- Moisture barrier requirements
- Light barrier requirements
- Gas barrier requirements
- Chemical properties



Choosing suitable polymer/blister packs

Materials of Construction / Type	Critical Properties	Area of use
PVC 200/250/350	Low barrier / Simple unit pack / Aesthetic	Stable products like Paracetamol, Co-trimoxazole, certain softgel capsules etc.,
PVC / PVdC (250/40)	Low barrier better than PVC	Products not very sensitive to moisture, gases and with moderate self life- Multivitamin tablets and capsules
PVC / PVdC (250/60)/ (250/90)/ (250/120)	Good barrier	Moderate to high sensitive range of products, certain FDC/ Enzyme products
PVC / PE / PVdC (200/25/60)/ (250/25/90)(300/30/90)	Good barrier	Quite high sensitive range of products – 4 FDC(RHZE)
Ultrasafe Duplex	High barrier/economical	Quite high sensitive range of products
Ultrasafe Triplex	High barrier/economical	Quite high sensitive range of products
PVC/Aclar (10μ to 100μ) PVC/COC, PE/COC	Excellent barrier	Extremely moisture sensitive range of products-
OPA/Al foil/PVC Alu/Alu	Excellent barrier	Extremely sensitive range of products – Cefuroxime Axetil tablets, Levocetirizine Tablets,
OPA/Al foil/PVC Alu/Alu with desiccant	Excellent barrier	Extremely moisture sensitive range of products
Aluminium foil with HSL (Hard tempered) 0.02 / 0.025	Excellent barrier	Lidding foil for blister packing
Aluminium foil (Hard tempered with special coating)	Excellent barrier	Lidding foil for COC
Aluminium foil / poly (30 –40 microns (soft tempered)	Excellent barrier	For strip packing use of very sensitive range of products – Omeprazole Capsules, Ranitidine Tablets etc.,
Aluminium foil / VMCH (30 –40 microns (soft tempered)	Excellent barrier	For strip packing use of dark colored sugar coated tablets.
Paper /Poly	Very low barrier / Simple unit pack / Aesthetic look	Very economical pack for very stable products.
Paper/Al/HSL	Excellent barrier	For Child resistance blisters pack

Choosing suitable polymer/blister packs

Comparative WVTR values of various blister films on flat sheet

(38 deg C/90% RH - g/m2/day)

Materials of Construction / Type	WVTR values (g/m2/day)
PVC 250	3
Polypropylene	1
PVC / PVdC (250/40)	0.75
PVC / PVdC (250/60)	0.5
PVC/10μ PCTFE (Aclar)	0.45
COC 190 μ	0.35
PVC/15μ PCTFE (Aclar)	0.36
PVC / PE / PVdC (250/25/90)	0.31
PVC/20μ PCTFE (Aclar)	0.27
COC 240 μ	0.28
COC 300 μ	0.23
PVC/23μ PCTFE (Aclar)	0.23
COC 350 μ	0.2
PVC/38μ PCTFE (Aclar)	0.15
PVC/51μ PCTFE (Aclar)	0.11
PVC/75μ PCTFE (Aclar)	0.08
PVC/102μ PCTFE (Aclar)	0.05
CFF (Alu/Alu) PVC/Alu45/OPA25	0

Choosing containers and closures

Materials of Construction / Type	Critical Properties	Area of use
HDPE container	Good barrier to moisture, gas and light	All kind of products from solid orals and dry syrup.
PET / PP (Amber)	Moderate barrier	Light sensitive products
Glass Bottles	High barrier	For highly sensitive products
Glass vials (USP I and II)	High barrier	For injectables product
Glass bottles and vials (USP type III)	High barrier	Dry syrup, suspensions and powder for injection.
Surface coated vials	High barrier	Sensitive products
PFS (glass/ PE)	Moderate to high	For unit dose injectables
Rubber stopper, natural rubber butyl, Halobutyl.	Chemical resistant, low permeability, low water/solvent	Injectable products
Rubber stopper, natural rubber butyl, Halobutyl (legged and slotted)	Chemical resistant, low permeability, low water/solvent	Lyo injectable products
Desiccant	Desiccant will effectively alleviate moisture and odor problems.	
1. Silicagel bags (Tyvek packs and canisters)		1. Moisture sensitive products
2. Activated Carbon		2. Product release odor / gas
3. Molecular sieves		3. Highly moisture sensitive products

Choosing containers and closures

- COMPARATIVE OTR VALUES

Materials of Construction / Type	OTR values (g.mm/(m2/day))
LDPE	241
HDPE	102
Polystyrene	127
Polycarbonate	114
Poly propylene	89
PVC	4
PET	2

Choosing appropriate primary pack

Desiccants have been utilised to control the exposure of products to the ingress of moisture.

Desiccants vary in their capacity and the rate that they adsorb/absorb ingressed moisture.

Silica gel is very efficient at absorbing moisture at high relative humidity, but comparatively poor at lower Relative Humidity.

Molecular sieve desiccants - the opposite scenario prevails.

As a consequence, more molecular sieve is required at higher relative humidity, and the greater the handling precautions that are required during packaging operations.

Based on the calculated WVTR of known container components and the rate of moisture adsorbed by desiccants, the amount of desiccant that would be required to maintain a specified relative humidity over the product's shelf-life can be determined and used.

TESTING AND STABILITY

Critical parameters during screening

- Release of chemicals from components of packaging material
- Release of visible and /or sub-visible particles
- Adsorption or absorption of pharmaceutical components by packaging material
- Chemical reaction between pharmaceutical product and packaging material
- Degradation of packaging component in contact with pharmaceutical products
- Influence of manufacturing process on the container.

TESTING AND STABILITY

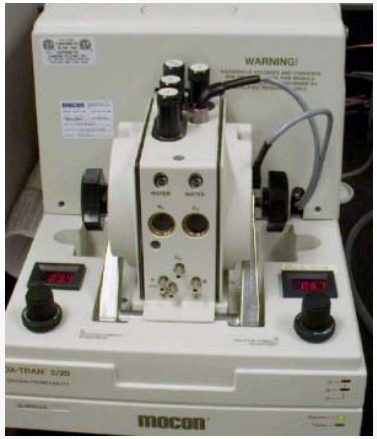
QC test - routine tests

- Vary according to the type of material used
- Visual inspection
- Identification test
- Dimensional test
- Physical tests
- Chemical tests
- Microbiological tests

TESTING AND STABILITY

QC Plus (Qualification)

- What need to be looked in
- WVTR (water vapour transmission rate)
  - Flat film
  - Formed blister



- OTR
- Extractables and Leachables

- Periodic review and re qualification in case of major change and source change

TESTING AND STABILITY

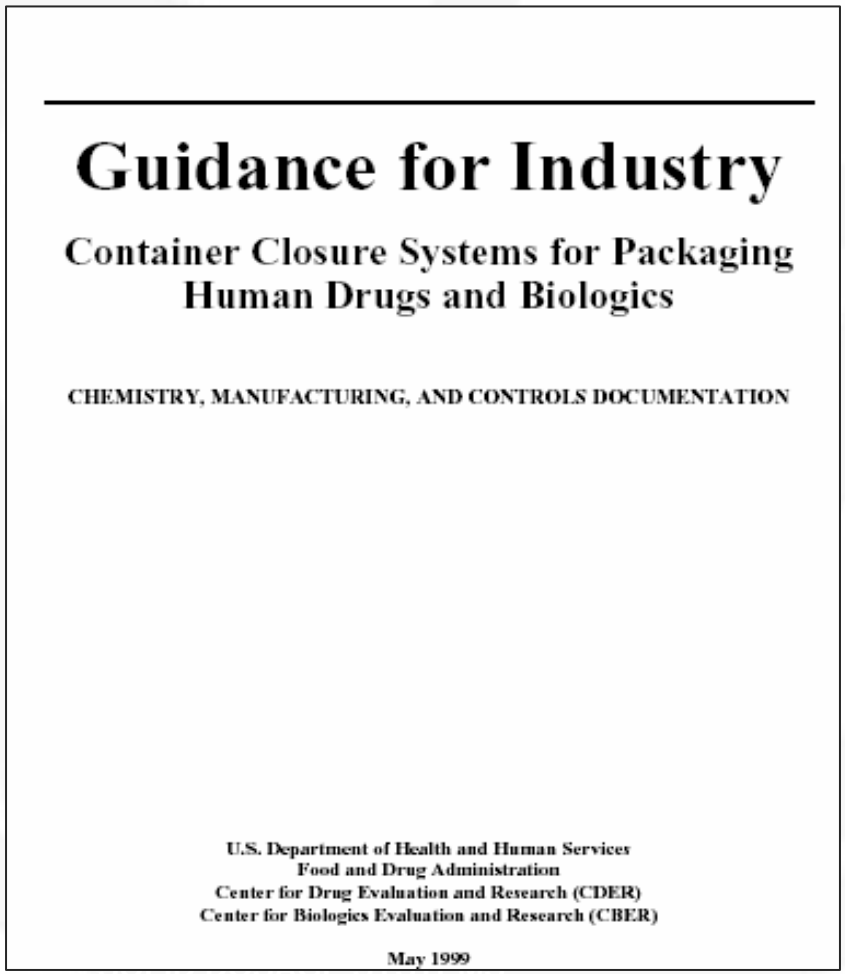
Packaging Integrity

A failure in an impervious container closure system can occur due to the failure in their seal integrity at the interface, which may affect the drug product stability due to ingress of moisture, oxygen or microbial contamination.

- Forming - can have impact on WVTR
- Sealing - pressure, temperature and dwell time - leads to increased permeability
- **Integrity testing :**
  - **Bubble test - Blister / strip pack, liquid bottles/cap**
  - **pressure decay test - vials, ampoules,Blister, pouches, IV bag**
  - **Vacuum decay test - Vial, Ampoules etc**

Regulatory (US)

Guidance for Industry, Container Closure Systems for Packaging of Human Drugs and Biologics



Guidance for Industry

Container Closure Systems for Packaging Human Drugs and Biologics

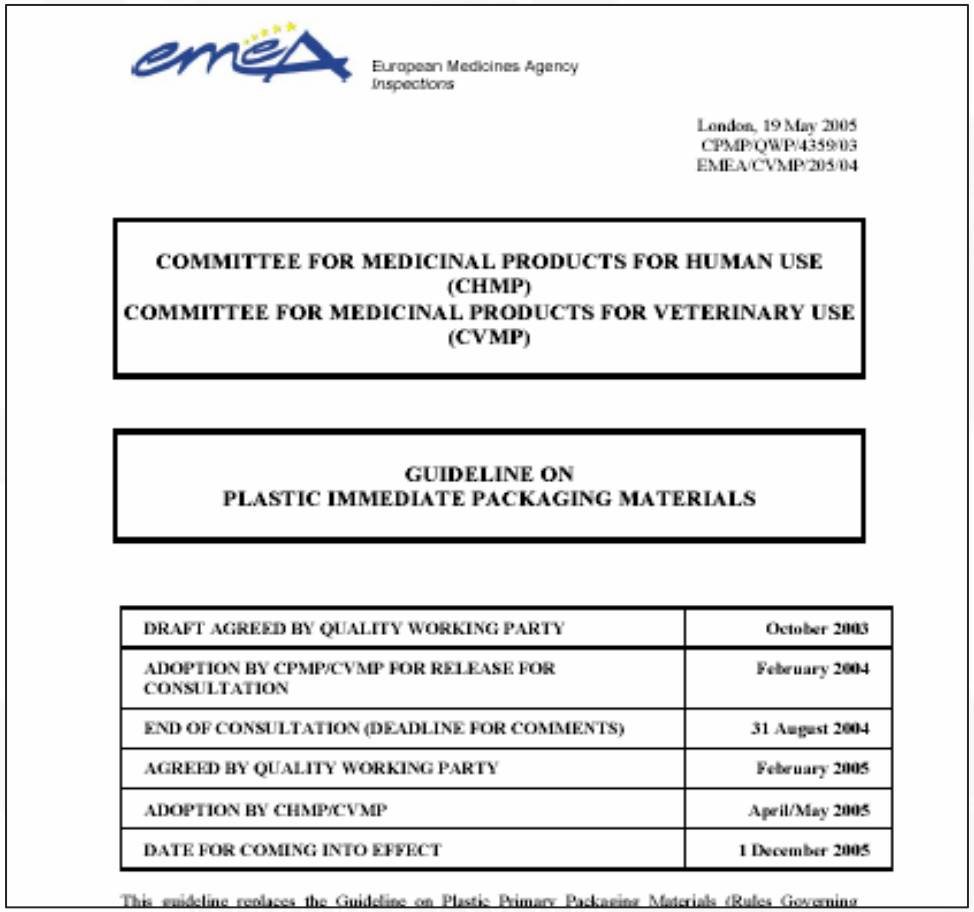
CHEMISTRY, MANUFACTURING, AND CONTROLS DOCUMENTATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 1999

Regulatory (Europe)

CPMP/QWP/4359/03 – Guideline on Plastic Immediate Packaging Materials - specific to plastics only



European Medicines Agency
Inspections

London, 19 May 2005
CPMP/QWP/4359/03
EMEA/CVMP/205/04

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)
COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

GUIDELINE ON
PLASTIC IMMEDIATE PACKAGING MATERIALS

DRAFT AGREED BY QUALITY WORKING PARTY	October 2003
ADOPTION BY CPMP/CVMP FOR RELEASE FOR CONSULTATION	February 2004
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 August 2004
AGREED BY QUALITY WORKING PARTY	February 2005
ADOPTION BY CHMP/CVMP	April/May 2005
DATE FOR COMING INTO EFFECT	1 December 2005

This guideline replaces the Guideline on Plastic Primary Packaging Materials (Rules Governing

Case Studies

- Strip packing of colored sugar coated tablets
- Selection of special vials for special products
- Improper design of blisters
- Importance of secondary packing

Thank You