Blister process in pharmaceutical industry
Blister process in the pharmaceutical industry

The blister was first used in the 50’s as a primary packing in the pharmaceutical industry.

A design developed by Shering Germany for a tablet to be used by women was the beginning of the blister.

With the advances in technology, the packing in blisters was applied to the many pharmaceutical products that we know today.

In this course we will see the concept of the process, some common problems and some useful tips.
Medicine packing requirements

Article 21, Part 211 del Code of Federal Regulations, Food and Drugs, states:

“the packing and closure of medicines can not be reactive, addictive, or absorbed to guarantee the safety, identity, efficiency, quality and purity of the drug beyond the oficial or stablished requirements. The sealing system should offer the adecuate protection against adverse external conditions expected during storage and use that could harm or contaminate the product”.
The blister as a primary packing

**Phisical and Chemical** barrier that protects the product against external agents.
Advantages in the use of blister:

1) Product integrity
2) Protection of product
3) Tamper proof
4) Low possibility of accidental overdose
5) Compliance with patient favoring guidelines
6) Generation of identifiable single doses
Tipical process

1. Forming
2. Product loading
3. Sealing
4. Coding
5. Perforation
6. Cut
Forming materials

.- Thermoforming:

Single layer: PVC
Multilayer: PVC + PVdC
PVC + PCTFE (Aclar)

.- Coldforming:

Multilayer: Cold Forming Foil

Material selection criteria:

Product been packed.
Environment.
Marketing and sales.
Costs.
Available equipment.
Heat forming

Termo formable materials: Thermo plastic polymers PVC / PVDC / ACLAR®

Definition: union of hundreds of thousands of small molecules “monómers” that form huge chains.

Amorphous structure

Cristalline structure
PVC (PolyVinyl Chloride)

.- It is the most widely used due to its cost/protection ratio.

.- Its the material with the least protection.

.- It is used as the base for the rest of muti layers including Alu-Alu.

.- The blistering process is the most standard.
PVC + PVdC (PolyVinyl DiChloride )

- It is a two-layer material with PVC as a base, with an ayer of PVdC.

- Depending on the thickness of the PVdC (from 60 g/m2) low to medium protection is obtained.

- Special care in design and construction of tooling. Heating plates to be lined with non-stick surface.

- Toxic and corrosive gases (HCl) are produced during heating.

- As two materials are involved, different temperatures are to be chosen in each side of the heating plates.

- Forming plug-assist is recommended.
PVC + PCTFE (Policlorotrifluoretileno – Aclar)

.- It is a two layer material with PVC as base and an additional layer of Aclar.

.- Depending on the thickness of the Aclar layer (from 15 microns) medium to high protection is achieved.

.- Special care in design and construction of tooling. Heating plates to be lined with non-stick surface.

.- As two materials are involved, different temperatures are to be chosen in each side of the heating plates.

.- Forming plug-assist is recommended.
Thermoforming

Thermoplastics → The temperature is raised to enable forming

Contact

Heating plates

Heating coils

Tunnel

Neopackaging
Blister Industry
Thermoforming

1. Transitory deformation
2. Molecular movility
3. Transitory deformation
4. Permanent deformation
Thermoforming
Positive air pressure
Plug-assisted forming.
Cold forming foil.

.- It is a multi-layer material whose main component is aluminum.

.- Gives the best protection.

.- The film is composed of PVC (inside layer of the blister), OPA and adhesives.

.- The PVC and OPA give better forming and structural characteristics to aluminum.
Cold forming
Fisures in Alu-Alu blisters

Fisure causes:

- Excessive stretching.
- Tooling defects.
- Wrong set up.
- Material problems.

(25 µm fisure)
Comparison between cold forming Vs. thermoforming.

Size differences in **thermoplastic** vs. **alu cold forming**
Comparing cold forming Vs. Thermoforming.

.- Less efficient process.

.- Bigger alveoluses → Bigger blisters → Less blister per cycle.
   → less tablets per blister.

.- More complex forming means less speed.

.- Need to have microfisures detection hardware

.- More complex loading → Manual loading is slow and inefficient.
   → More expensive mechanical loading devices.

.- No visual inspection can be done once the blister is sealed.

.- Blister fragility.
Product feeding

To be considered:
1. Batch size
2. Type of product / characteristics
3. Blister design/ geometry / graphics
4. Type of barrier (PVC, Aclar®, Alu Alu)
5. Powder / aspiration

Alternatives:
1. Manual feeding
2. Semi-automatic feeder
3. Universal automatic feeder
4. Dedicated automatic feeder
• Manual

Vacuum

manifold
• Semi-automatic feeder
• Automatic Universal Feeder
Sealing

The base and sealing material are sealed by pressure and temperature.
Lidding material (Alumminum).
Thermosealing laquers

The functional characteristics of the lacquer is to act as a thermosealing agent between the PVC or PVDC and the lidding material.

It is a critical component as it has to assure:

- **Intimate sealing between PVC and aluminunum**
  *(hermeticity)*

- **Sealing at relatively low temperatures**
  *(inks, barnishes and product degradation)*

- **Dimensional stability**
  *(deformation)*

- **Dstability in time of the union**
  *(aging)*

- **Inocuity**
  *(Tablet contamination from solvents or decomposition of polymers into free monomers)*
Sealing

Thermosealing lacquer

P, T, t

Forming material (PVC o PVDC)
Coding

CUÑO TIPO "T"

DISEÑO SELLO

DISEÑO NO SELLO
Perforation

One way

Two way
Die-Cutting
Simple efect
Cut

Doble efect

(Saves material)
Main accessories and optionals

- Plug-Assisted forming system.
- Cold forming system.
- Pin-Hole detector.
- Feeders.
- Print mark registrarion - Fotocentering device (centered printing).
- In-line printer.
- Filling Inspection Systems.
- Blister positioner
- Exit conveyor belt.
- Rejection sistem
- Others
  - Bar code reader.
  - Assisted sealing.
Photo centering – Mark reader and step corrector

The blister uses lidding material with centered printing.
Ej: Monodose
Medical samples.
Etc.
Photo centering – Mark reader and step corrector

1. Step is longer than the nominal for the lidding material. Mark moves downward.

2. Moves forward with the same step: the light is outside the mark. Sensor sends a signal: the corrector is activated.

3. The step corrector shortens the advance distance. The mark returns to the original position.

La impresión constantemente se desplaza respecto del corte, dentro de valores determinados.
In-line printer.

- Lidding material is blank. It is printed directly before sealing.
- More efficient stock management.

Printer types.

- Flexographic.
- Thermal transfer.
Load inspection systems.

Vision inspection are the most widely used.

Capable of verifying presence, position, colour and broken tablets.

Must be used along with the blister positioner and some rejection system.
Blister positioner

Prevents the blister from being retained in the die-cutting tool
If a vacuum-actuated suction cup system is included, it places them on the exit belt helping reject and transfer
Discard.

- **Complete step**
  - Discards all the blister in 1 step.

- **Individual**
  - Discards only the faulty blister.

- **Pick and Place**
  - The concept is not to reject the bad ones but to take the good ones at the end of the operation.

- **Discard control.**
  - Sensors verify that discard is done.
Blister design