# PDA VIRTUAL TRAINING COURSE

## EXTRACTABLES – LEACHABLES

# POLYMERS 101

**Trainer: Dr. Piet Christiaens, Nelson Labs Europe**

# Outline

**1. What is a polymer?**

2. Classification of polymers
    - *natural vs synthetic polymers*
    - *thermoplast vs thermoset polymers*
    - *homo-, co-, cross-linked and grafted polymers*
    - *polymerisation mechanism*

3. Properties of polymers
    - *morphology*
    - *glass transition temperature*

4. Composition of commercial polymers
    - *additives*
    - *residues*
    - *catalysts*
    - *oligomers*
    - *degradation compounds*

# 1. What is a Polymer?

A **polymer** is a chemical compound or mixture of compounds consisting of repeating structural units created through a process of polymerization

**Greek words**:

**πολύς** (polus, meaning "many, much")

**μέρος** (meros, meaning "parts")

Refers to a molecule whose structure is composed of **multiple repeating units**

As a consequence:

- o a characteristic of high relative molecular mass and
- o associated properties

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  - ***polymerisation mechanism***

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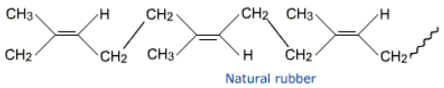
# 2. Classification of Polymers

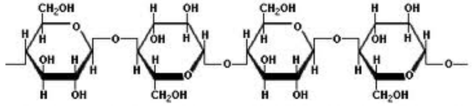
## NATURAL POLYMERS:

polymers also exist in nature

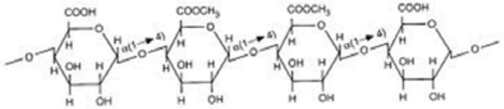
- Latex / natural rubber
- Starch
- Cellulose
- Pectin
- Silk / Wool
- DNA
- ....



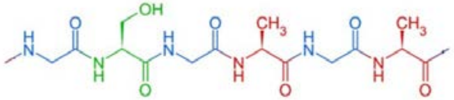
Repeating Isoprene units



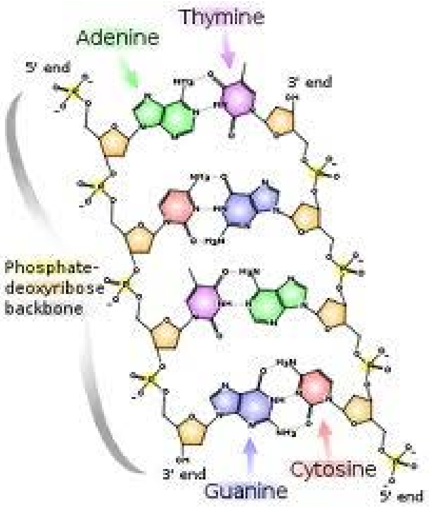
Repeating D-Glucose units



Repeating Galacturonic acid units



Repeating units of amino acids



DNA

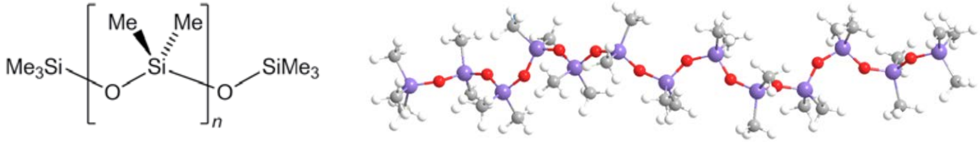
However, most of the pharmaceutical applications are with **SYNTHETIC POLYMERS**

# 2. Classification of Polymers

## SYNTHETIC POLYMERS

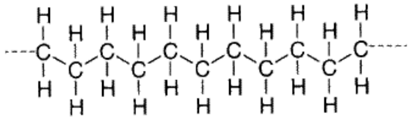
A small fraction are ***INORGANIC POLYMERS***

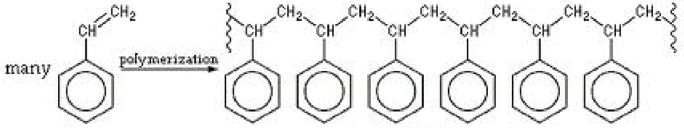
*Example: Siloxanes (PolyDiMethylSiloxanes; PDMS) (SILICONE)*



However, most of the polymers are ***ORGANIC POLYMERS***

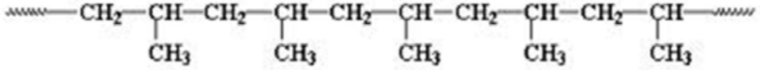
*Examples: polyethylene (PE), polypropylene (PP), ethylene vinyl acetate (EVA), polystyrene (PS), Isobutylene Isoprene Rubber (IIR rubber), nylon 6, nylon 6,6,...*

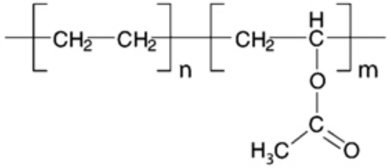


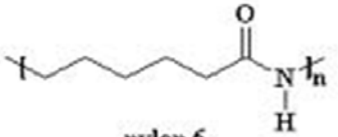


styrene

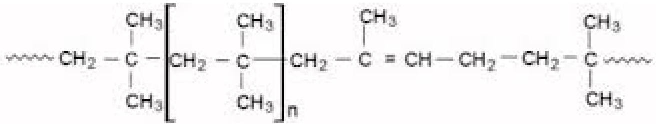
polystyrene

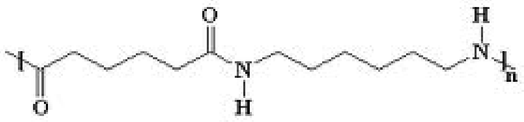






nylon 6

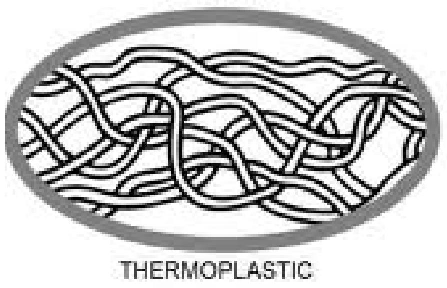




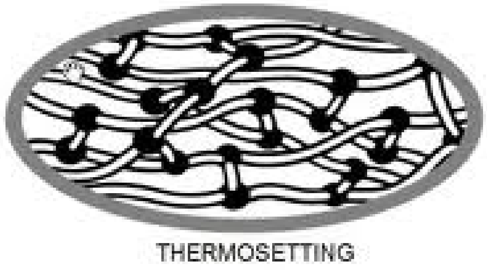
nylon 6,6

# 2. Classification of Polymers

## THERMOPLAST VERSUS THERMOSET



“Entangled” polymer chains

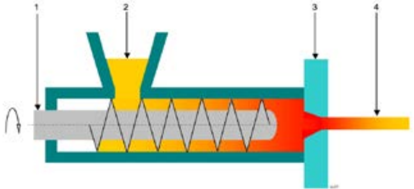


Crosslinked polymer chains

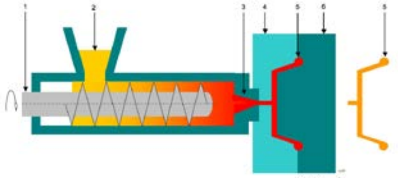
**THERMOPLAST:**

Polymers that soften when heated and become firm again when cooled

Giving the **final form to a container/component** is based upon this principle: extrusion, molding,...



*Extrusion*

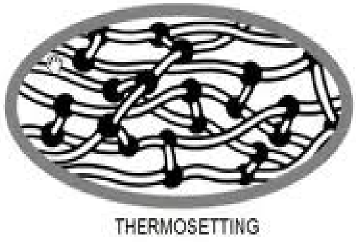


*Injection Molding*

*Examples: LDPE, HDPE, PP, EVA, PTFE, PC,...*

# 2. Classification of Polymers

**THERMOSET:**



Polymers that soften when heated and molded subsequently BUT <u>decompose</u> when reheated (i.e. cannot be reformed after cooling)

Thermoset polymers are typically "**<u>cross linked</u>**" (irreversible chemical bonds formed during curing process)

*Examples:* *Bakelite* *Rubbers* *Silicone tubings*

Fenol Formaldehyde Resin

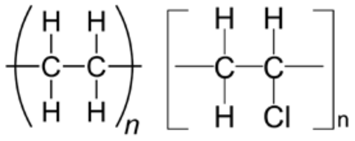
# 2. Classification of Polymers

## TYPE OF POLYMERS

**HOMOPOLYMER:** polymer built from a sequence of identical monomers

A-A-A-A-A-A-A-A-A-A-A-A-A-A

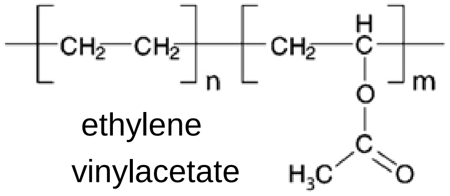
*Examples: PE, PP, PVC*



**COPOLYMER:** polymer built from a sequence of *two different monomers*

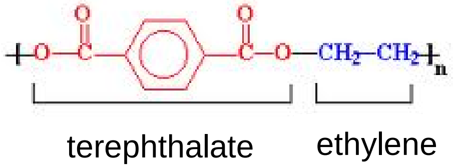
**Random** copolymer A-B-A-A-B-B-B-A-B-A-A-A-B

*Example: Poly EVA*



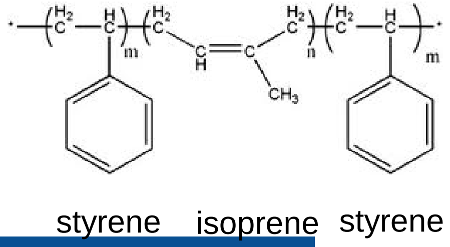
**Regular** copolymer A-B-A-B-A-B-A-B-A-B-A-B-A

*Example: PET*

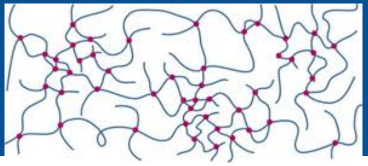


**Block** copolymer A-A-A-B-B-B-B-B-B-B-B-A-A

*Example: SIS elastomer*



# 2. Classification of Polymers

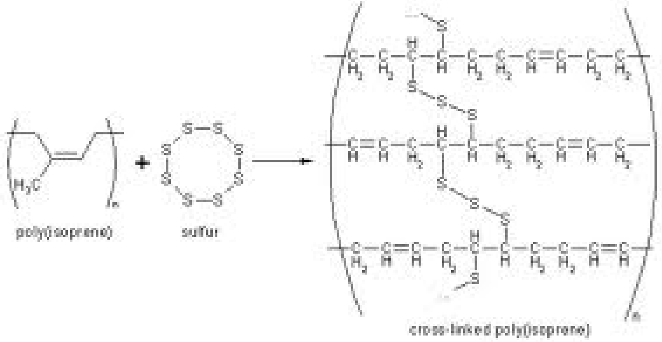


## CROSS-LINKED POLYMERS

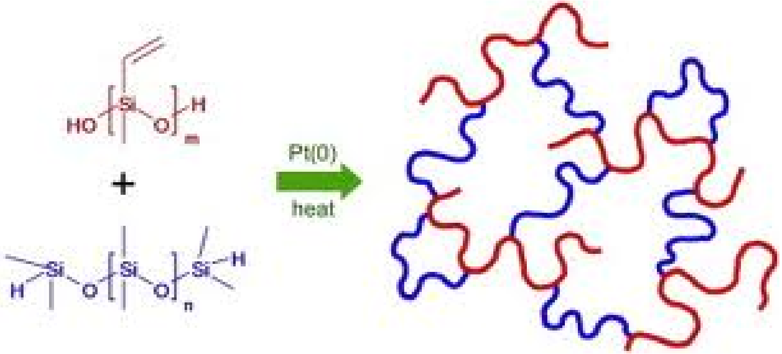
### (THERMO-SETS)

## EXAMPLES:

*Isoprene / butadiene rubbers*



*Silicone rubbers (Pt-cured)*

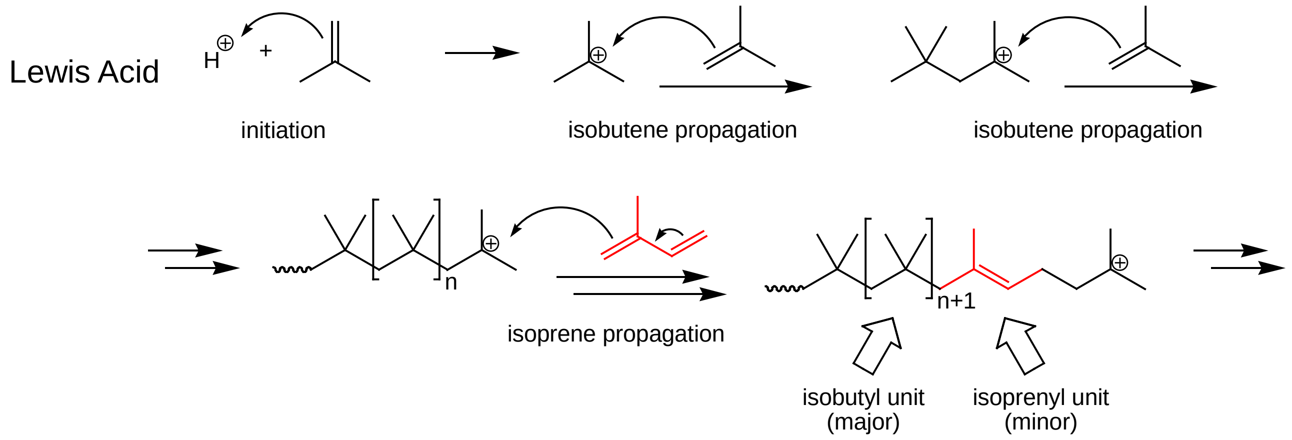


# 2. Classification of Polymers

## POLYMERIZATION MECHANISM

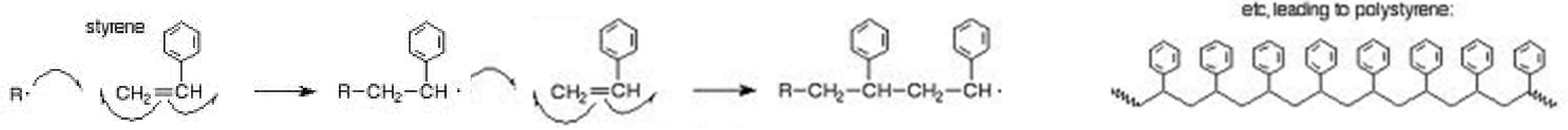
### CHAIN GROWTH:

### *Example 1: Cationic polymerization of "butyl elastomer"*



*Understanding polymerization of butyl elastomer helps to understand the formation and presence of rubber oligomers*

### *Example 2: Radical polymerization of polystyrene*

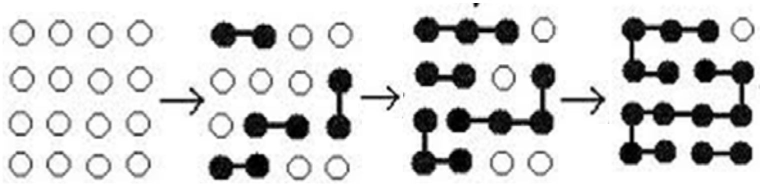


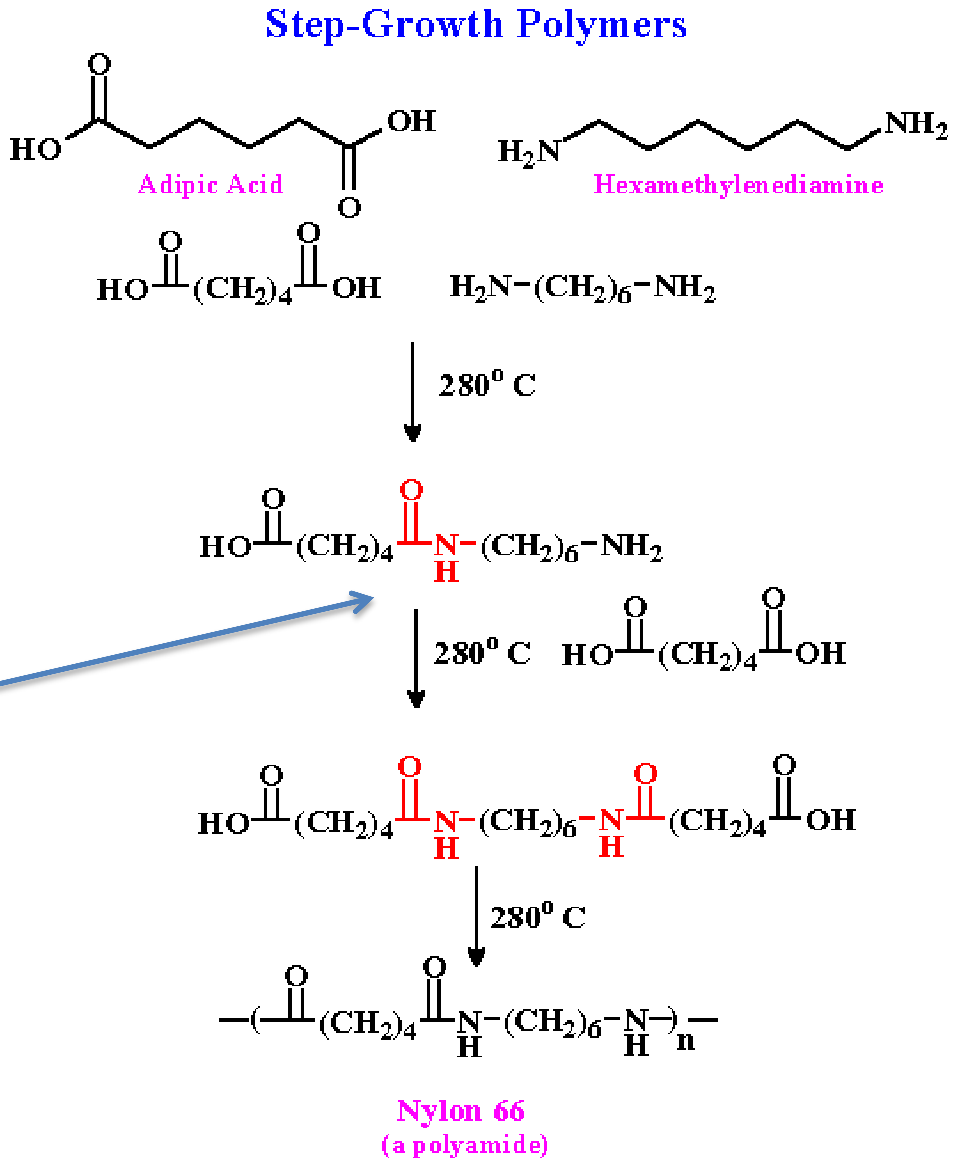
# 2. Classification of Polymers

## POLYMERIZATION MECHANISM

### STEP GROWTH:

*Example: Polycondensation – Nylon 6,6*





seen as an Extractable / Leachable

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**3. Properties of polymers**
    - ***morphology***
    - ***glass transition temperature***

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    - *additives*
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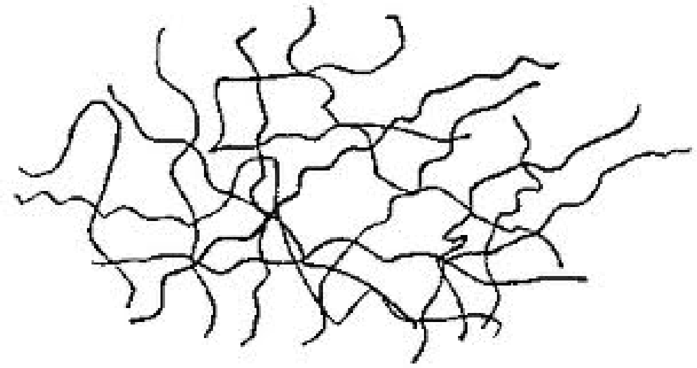
# 3. Properties of Polymers

## 1. MORPHOLOGY

### AMORPHOUS POLYMERS



Because of

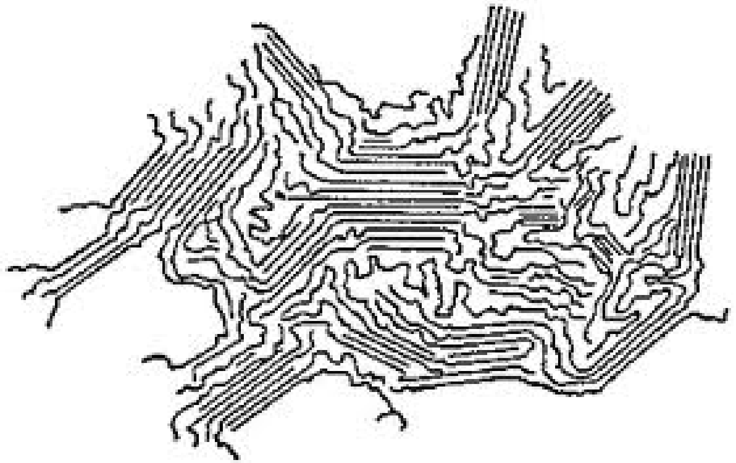
- Irregularities in polymer structure
- Nature of the polymer
- Cross-linking (for certain polymers)

*No intermolecular bonds (e.g. Hydrogen bonds, Van der Waals forces) will lead to an alignment of the polymer chains*

*Examples: PS, PVC, SAN, ABS, PMMA, PC, PES*

# 3. Properties of Polymers

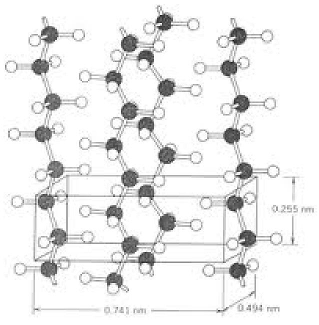
## 1. MORPHOLOGY



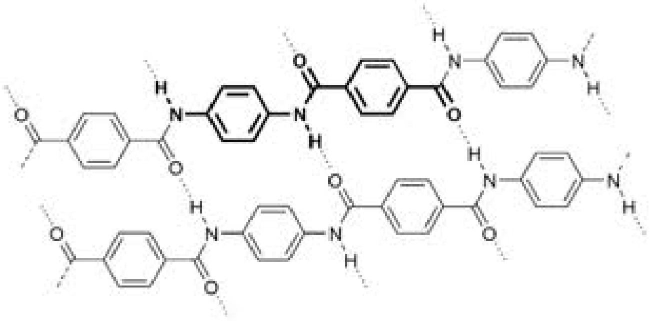
### (SEMI-)CRYSTALLINE POLYMERS

**Van der Waals forces** (e.g. polyolefins)
**Hydrogen bonds** (e.g. polyamide)
➔ Bring “alignment” in chains

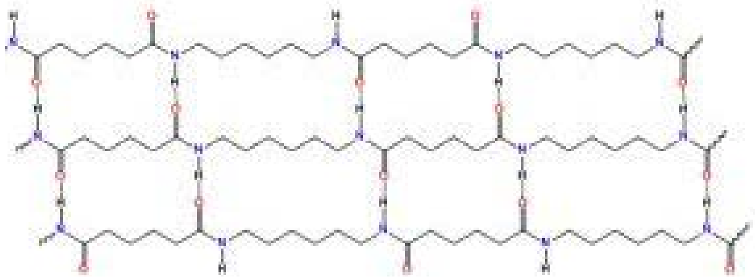
Impact of Stereochemistry of a polymer on physical properties



PE



Kevlar

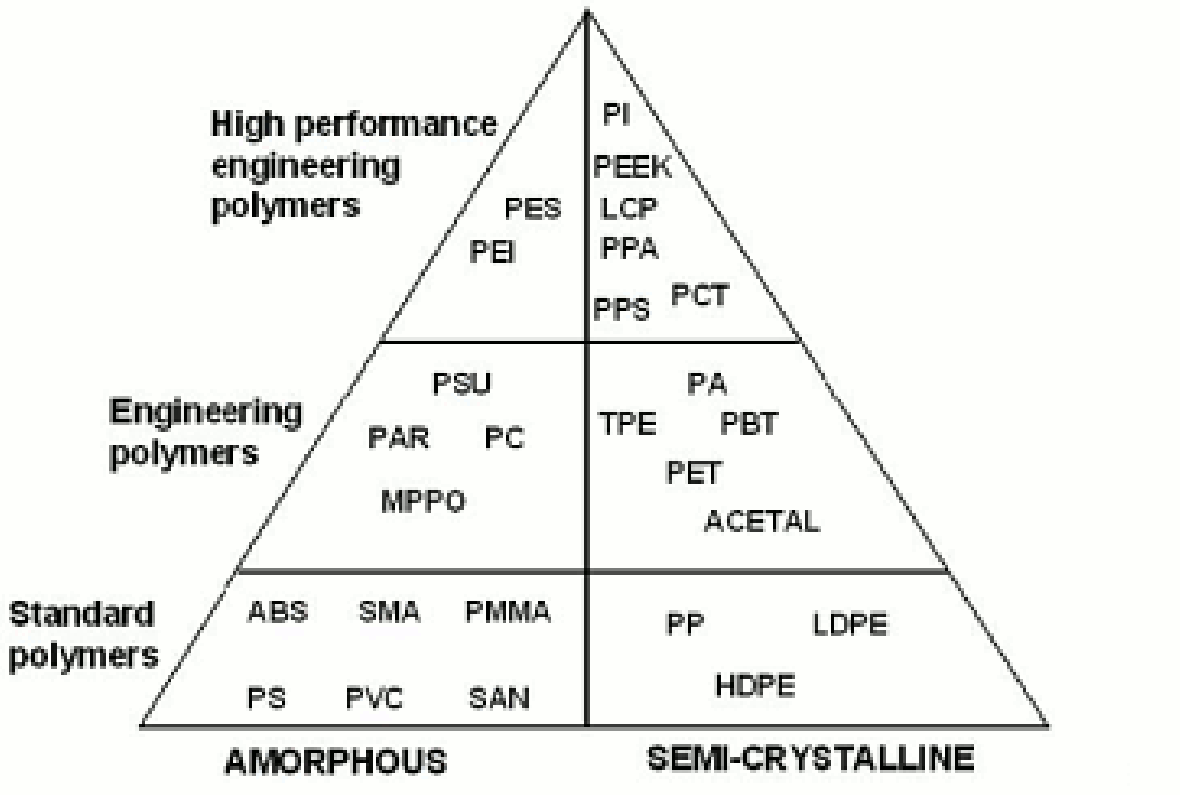


Nylon 6,6
(polyamide)

# 3. Properties of Polymers

## 1. MORPHOLOGY

AMORPHOUS VS. CRYSTALLINE

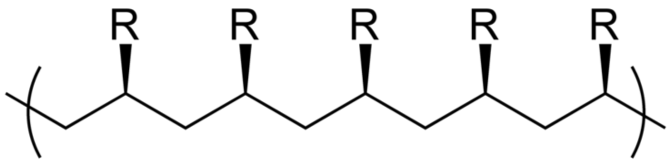


# 3. Properties of Polymers

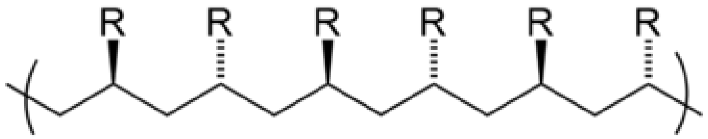
## 1. MORPHOLOGY

### AMORPHOUS VS. CRYSTALLINE

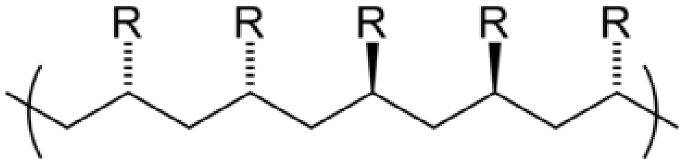
Impact of **StereoChemistry** of a polymer on physical properties



**Isotactic**
*Typically semi-crystalline*
*(e.g. PP via Ziegler-Natta polymerisation)*



**Syndiotactic**
*PS: Syndiotactic PS is semi-crystalline*



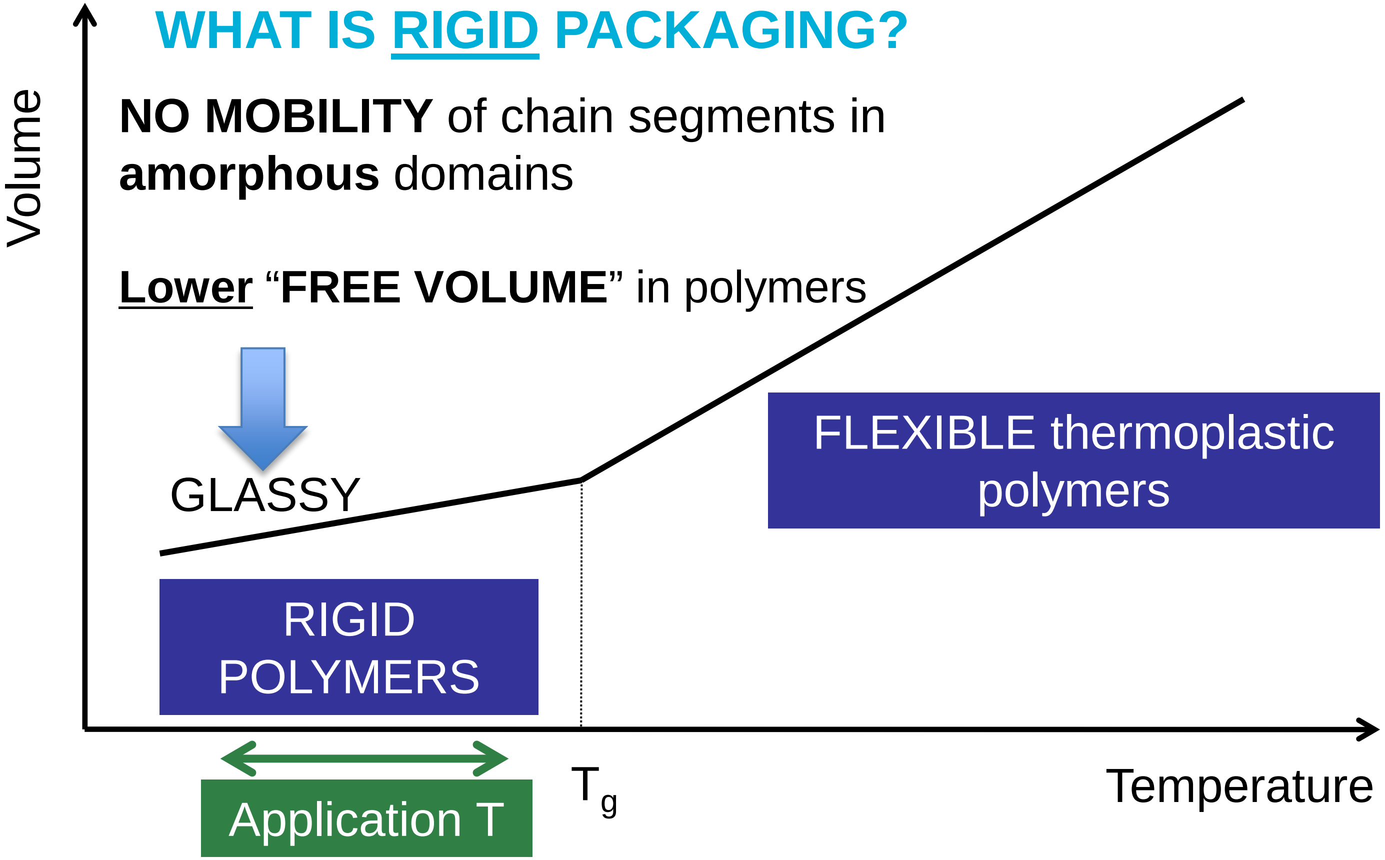
**Atactic**
*Typically amorphous polymers*
*PS: Atactic PS is amorphous*

**TACTICITY MODULATORS, SOMETIMES FOUND AS EXTRACTABLES**

# 3. Properties of Polymers

## 2. GLASS TRANSITION TEMPERATURE ($T_g$)

Temperature when a polymer goes from a “glassy” state ($< T_g$) to a “rubber” state ($> T_g$)



**WHAT IS RIGID PACKAGING?**

**NO MOBILITY** of chain segments in **amorphous** domains

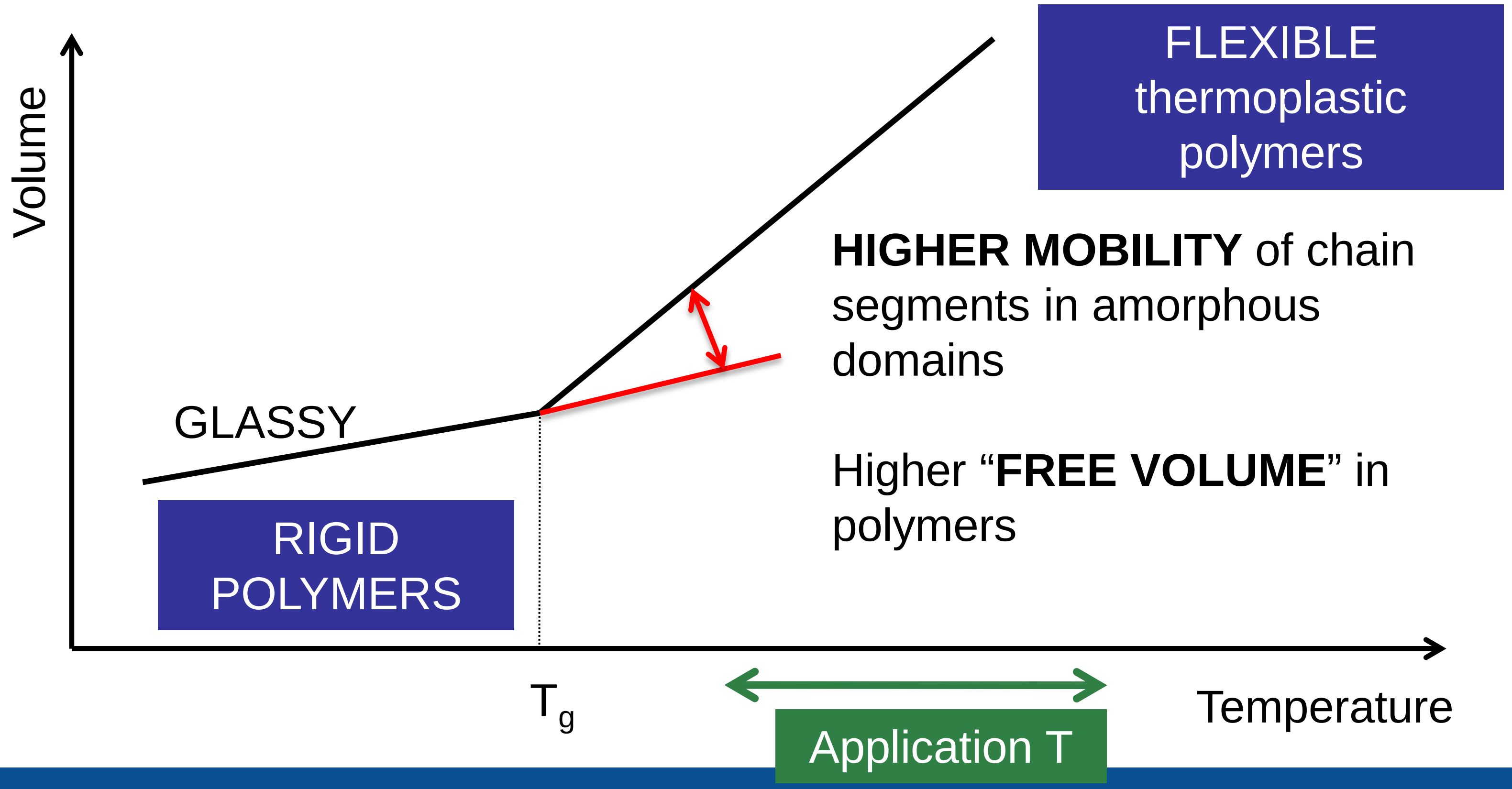
**Lower** “**FREE VOLUME**” in polymers

# 3. Properties of Polymers

## 2. GLASS TRANSITION TEMPERATURE ($T_g$)

Temperature when a polymer goes from a “glassy” state ($< T_g$) to a “rubber” state ($> T_g$)

### WHAT IS FLEXIBLE PACKAGING?



FLEXIBLE thermoplastic polymers

RIGID POLYMERS

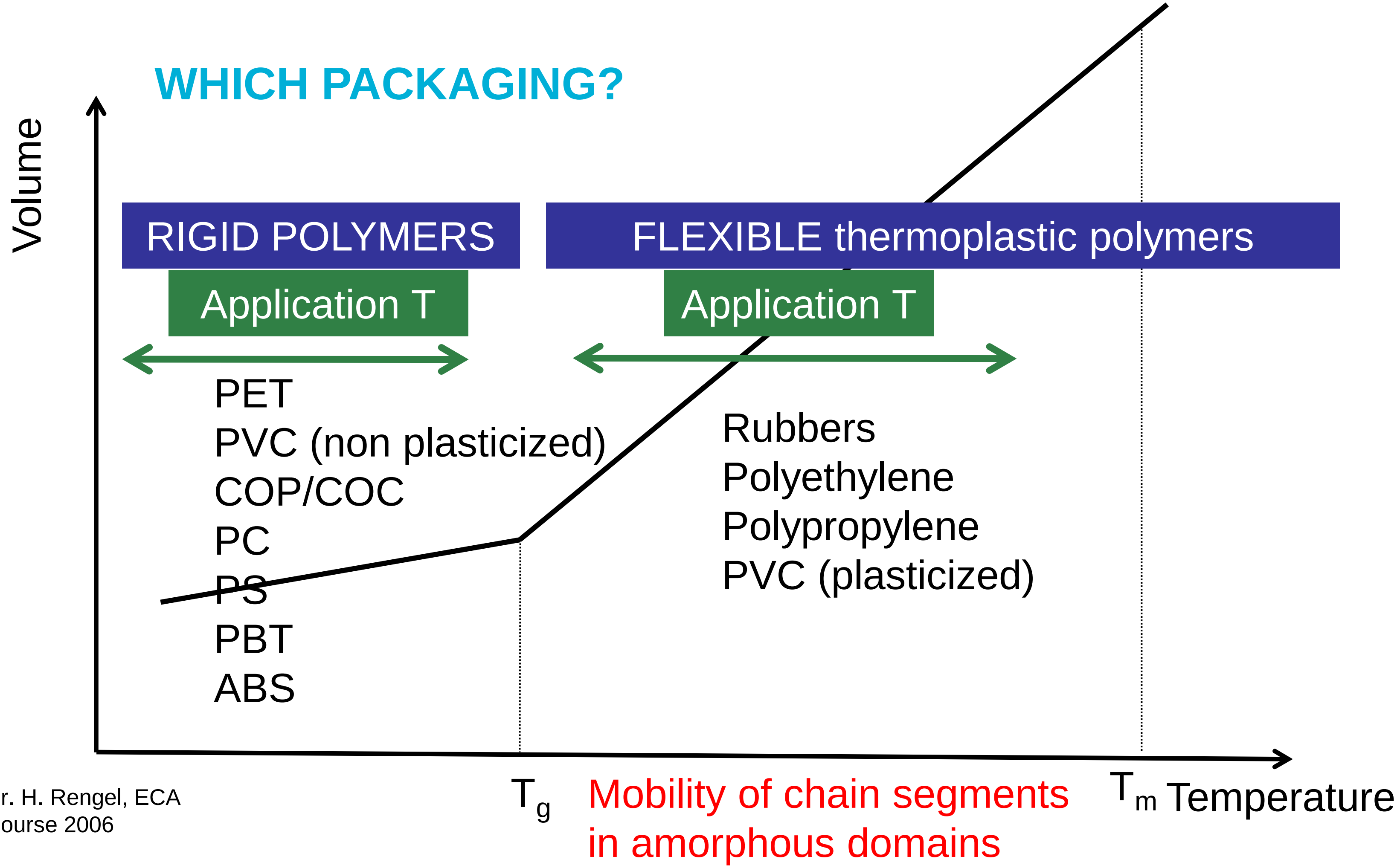
**HIGHER MOBILITY** of chain segments in amorphous domains

Higher “**FREE VOLUME**” in polymers

Application T

# 3. Properties of Polymers

## 2. GLASS TRANSITION TEMPERATURE ($T_g$)



**WHICH PACKAGING?**

**RIGID POLYMERS**

Application T

- PET
- PVC (non plasticized)
- COP/COC
- PC
- PS
- PBT
- ABS

**FLEXIBLE thermoplastic polymers**

Application T

- Rubbers
- Polyethylene
- Polypropylene
- PVC (plasticized)

Mobility of chain segments in amorphous domains

Dr. H. Rengel, ECA
Course 2006

# 3. Properties of Polymers

## 2. GLASS TRANSITION TEMPERATURE ($T_g$)

Examples of $T_g$ for different materials

LDPE $T_g$ = -125° C
POM $T_g$ = -50° C
PP $T_g$ = -25° C

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PBT $T_g$ = +70° C
PVC $T_g$ = +81° C (non plasticized)
ABS $T_g$ = +110° C
PC $T_g$ = +150° C

*The $T_g$ of a material will also have an impact on the migration behavior of a material!*

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   - ***catalysts***
   - ***oligomers***
   - ***degradation compounds***

# 4. Composition of Commercial Polymers

Compounds

INTENTIONALLY ADDED

to a Polymer

*(functionality, protection, processability...)*

# 4. Composition of Commercial Polymers

**Anti-oxidants**
**Plasticizers**
**Photostabilizers**
**Slip agents**
Antiozonants
Coupling agents
Lubricants
**Acid scavengers**
Peroxides / crosslinkers

Blowing agents
**Pigments / colorants**
Antistatic agents
Metal chelators
Adhesives
**Catalysts**
**Clarifying agents**
Antifogging agents
Fillers

*(blue: coming with some examples)*

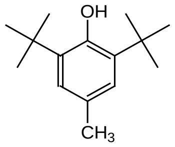
# 4. Composition of Commercial Polymers

## Anti-oxidants

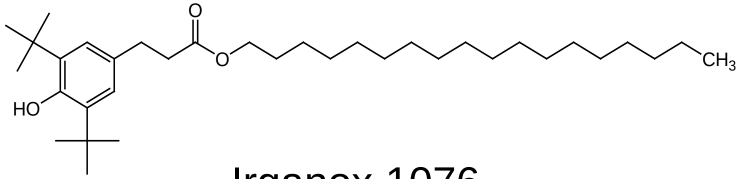
Function: assuring protection against thermal and oxidative degradation during processing and during shelf life of polymer

(*Sterically Hindered Phenols & Organic Phosphites/Phosphonates are mostly used*)

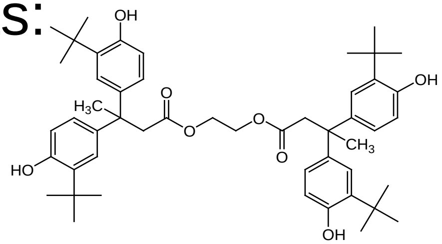
European Pharmacopoeia lists a.o. the following anti-oxidants:



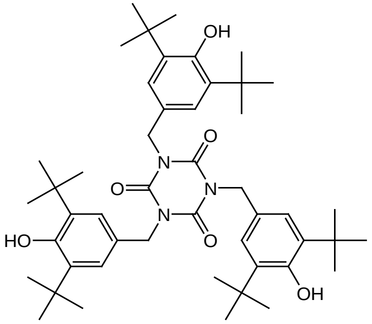
BHT



Irganox 1076



Hostanox 03



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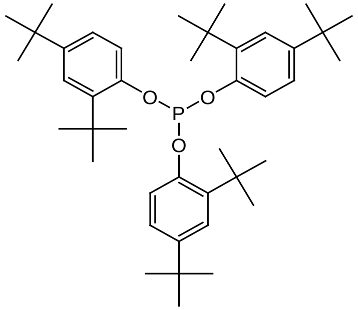
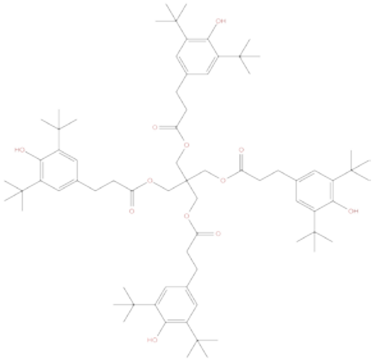
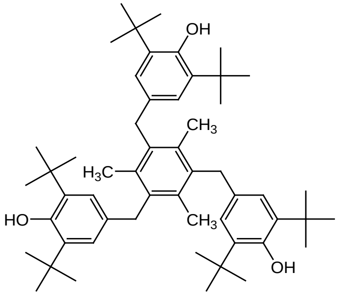


Irgafos 168



Irganox 1010



Irganox 1330

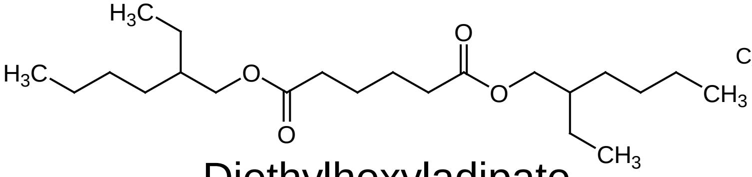
# 4. Composition of Commercial Polymers

## Plasticizers

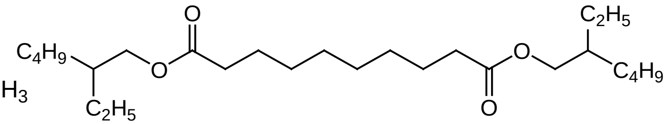
Function: gives the plastic flexibility and durability

Plasticizer requirements:

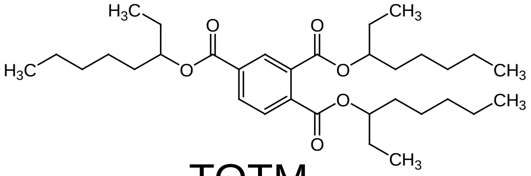
- *Low water solubility (low extractibility)*
- *Stability to heat and light*
- *Low odor, taste and toxicity*



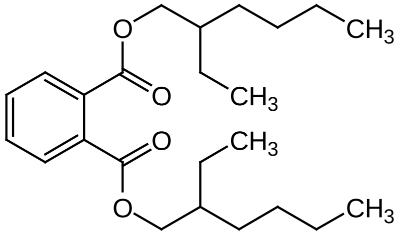
Diethylhexyladipate



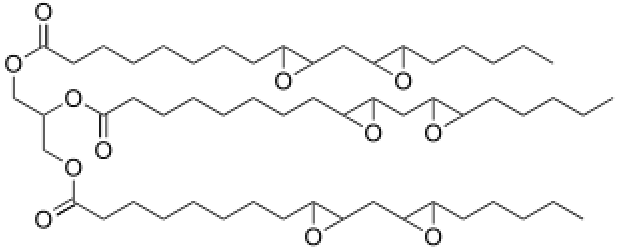
Diethylhexylsebacate



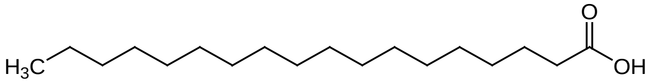
TOTM



Diethylhexylphthalate (DEHP)



ESBO

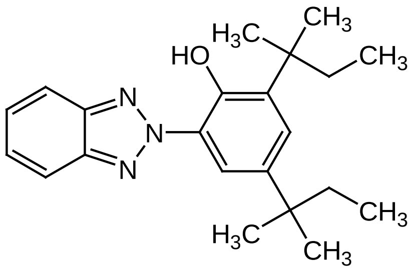


Stearic acid

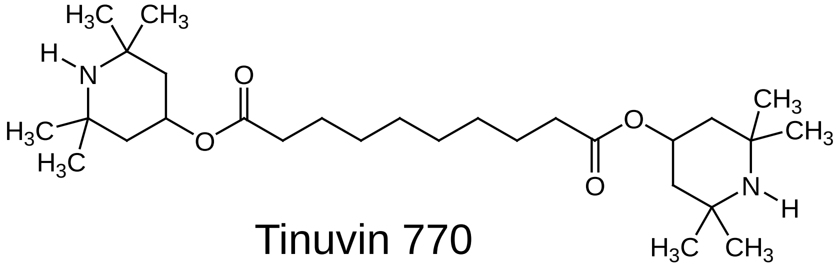
# 4. Composition of Commercial Polymers

## Photostabilizers

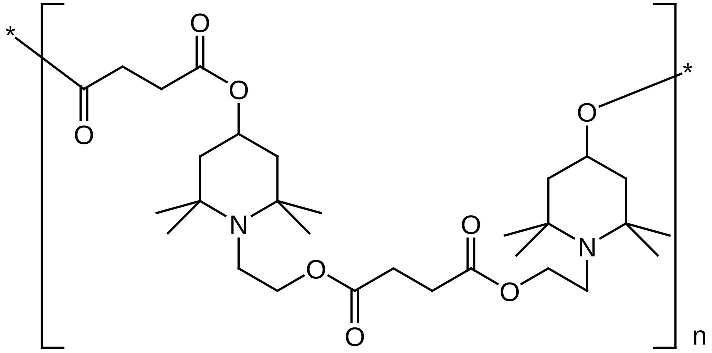
Function: protects the polymer from UV-Degradation (exposure to sunlight)



Tinuvin 328



Tinuvin 770

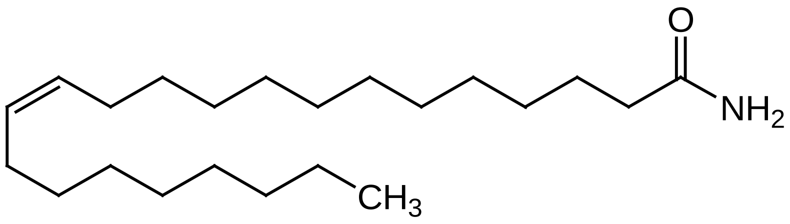


Tinuvin 622

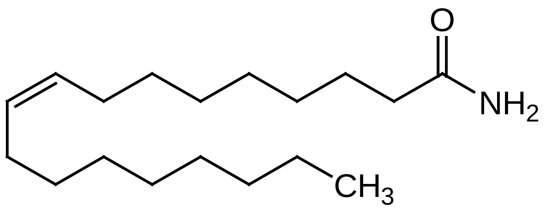
# 4. Composition of Commercial Polymers

## Slip agents

Function: reduce the “friction” or “film adherence”, important when producing bags from films



Erucamide (C22)



Oleamide (C18)

*Remark:*
*because of their specific properties, slip agents will be widely detected as Leachables!*

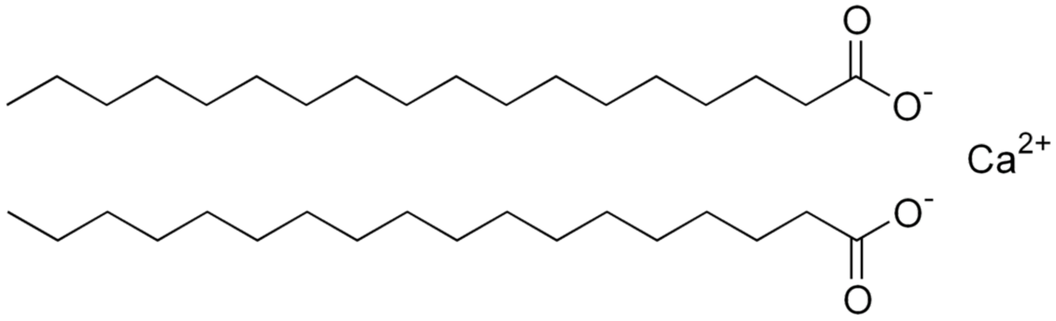
# 4. Composition of Commercial Polymers

## Acid scavengers

Function: Protects the polymer from “acid attacks” through conversion of strong acids (high degradation impact) to weak acids (low degradation impact)

*Example*: $Ca(Stearate)_2$ + 2HCl ➔ $CaCl_2$ + stearic acid

***strong acid*** ***weak acid***

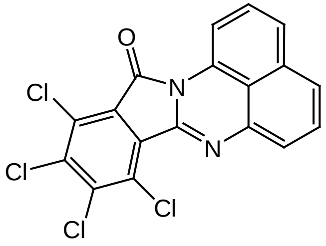


# 4. Composition of Commercial Polymers

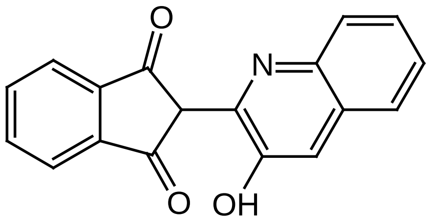
## Pigments / colorants

Function: Gives the polymer / rubber the desired color (cosmetic)

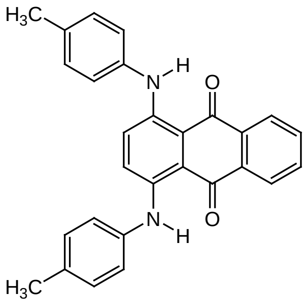
*Examples*: Carbon Black (PNA’s!), $TiO_2$ (white), $Fe_2O_3$ (red), Pigment Green 07



Solvent Red



Solvent yellow 114



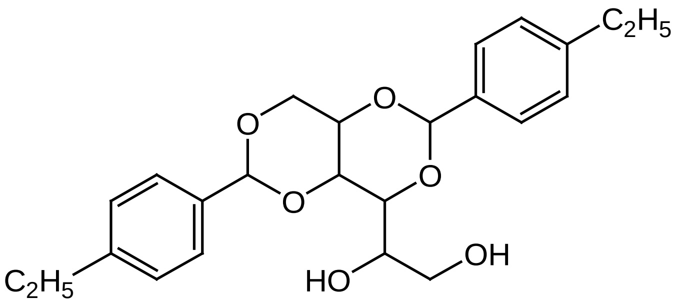
Solvent Green 03

***Remark*: beware of the composition of the masterbatch!**

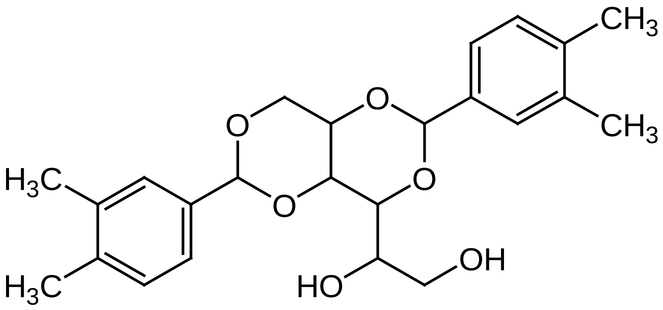
# 4. Composition of Commercial Polymers

## Clarifying agents (nucleating agents)

Function: by controlling the crystallisation (nucleation) when cooling off polypropylene, PP becomes transparent instead of opaque



NC-4



Millad 3988

# 4. Composition of Commercial Polymers

Compounds

UNINTENTIONALLY PRESENT

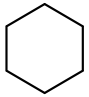
in a Polymer

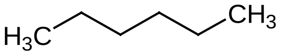
*NIAS: Non Intentionally Added Substances*

# 4. Composition of Commercial Polymers

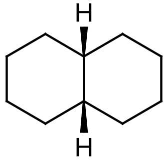
**Residues:** Residues from the production process (non-limitative)

## Solvents

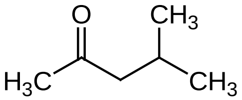

*Cyclohexane*



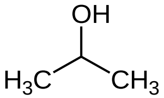
*Hexane*



*DHN*

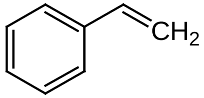


*MIBK*

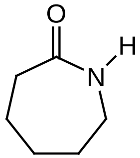


*IPA*

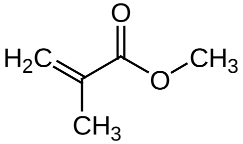
## Monomers



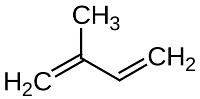
*Styrene*



*Caprolactam*



*Methyl methacrylate*



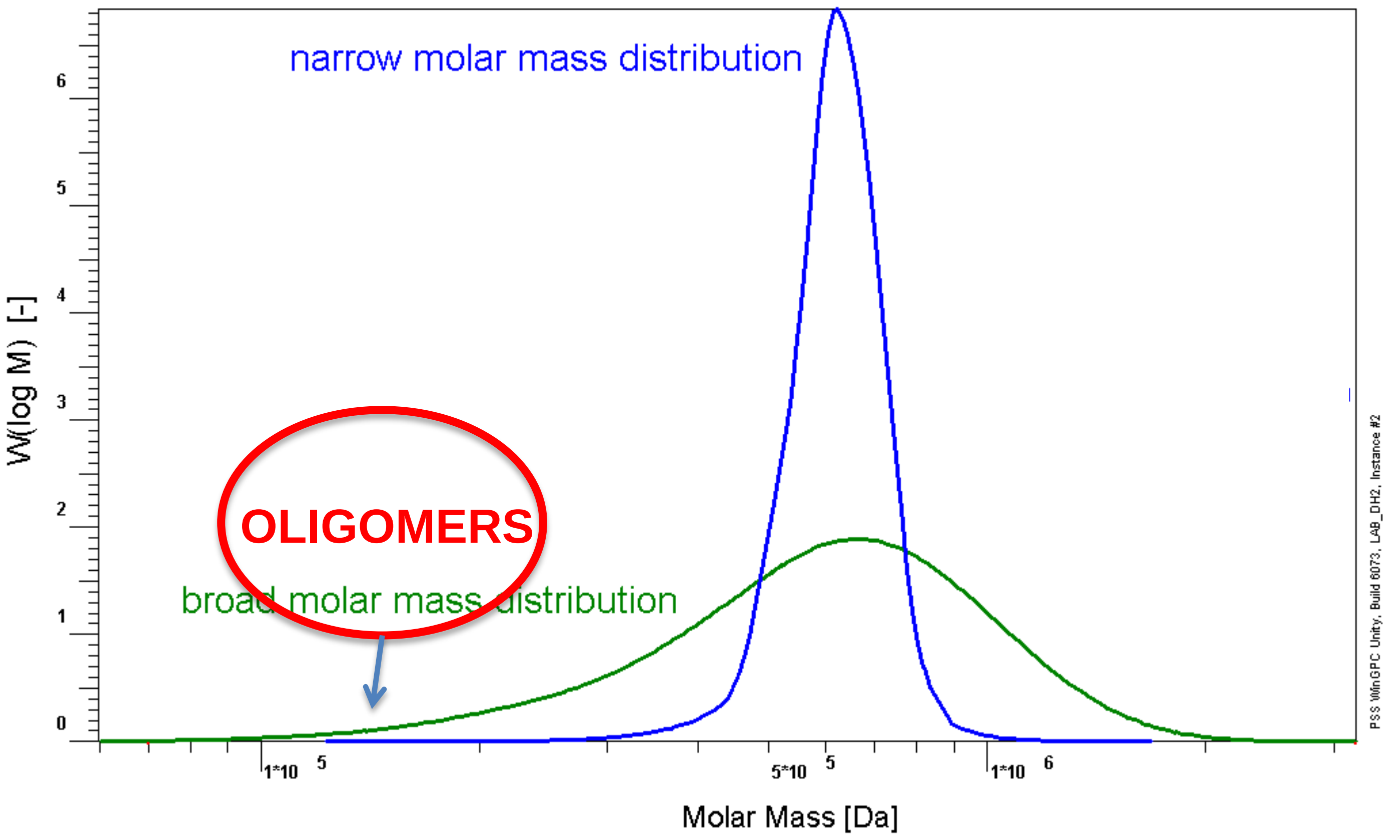
*Isoprene*

## Catalysts

Titanium
Zirkonium
Cobalt
Aluminum
Iron
Hafnium
...

# 4. Composition of Commercial Polymers

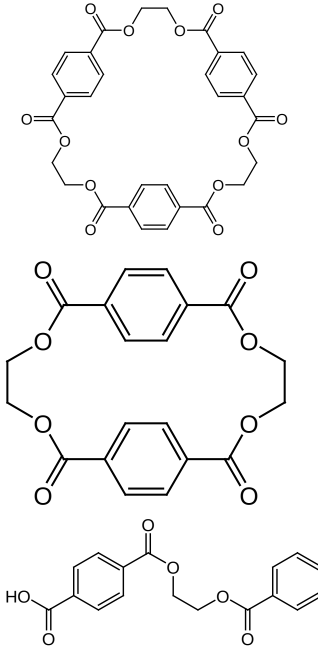
## Oligomers:

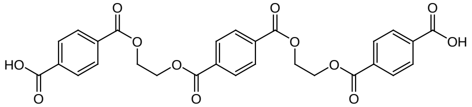


# 4. Composition of Commercial Polymers

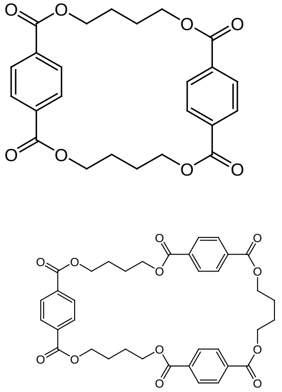
## Oligomers: examples

PET

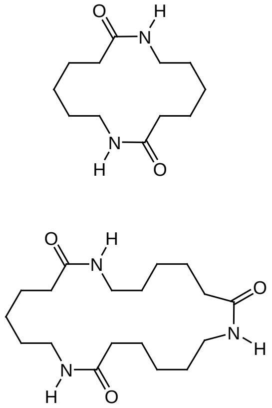




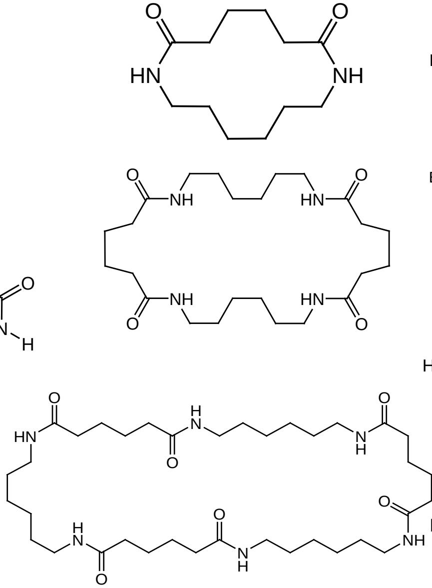
PBT



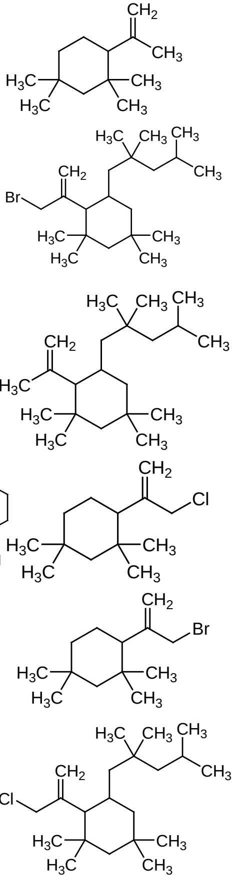
Nylon 6



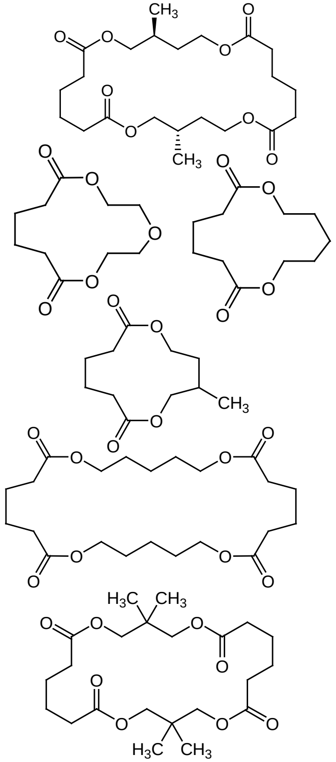
Nylon 6,6



Butyl Rubber



Polyester adhesive



+ Oxidation, Hydrolysis and degradation compounds of Oligomers

Other typical oligomers from Silicone, PP, PE, adhesives,...

# 4. Composition of Commercial Polymers

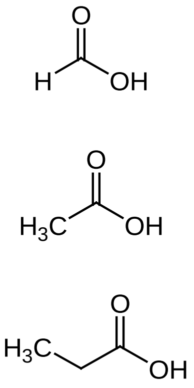
## Polymer degradation compounds:

Origin: Oxidative degradation of the polymers

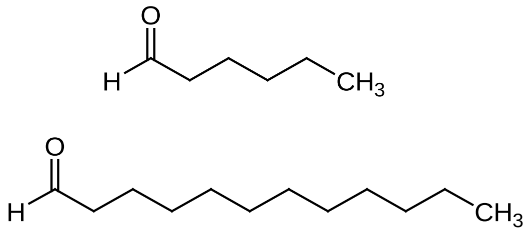
(when the polymer is not properly stabilized via anti-oxidants)

Example of polymer degradation compounds from **polypropylene**

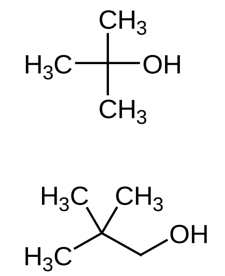
Acids



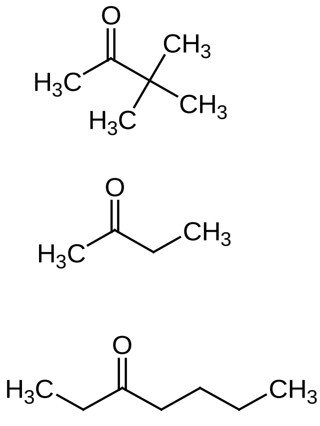
Aldehydes



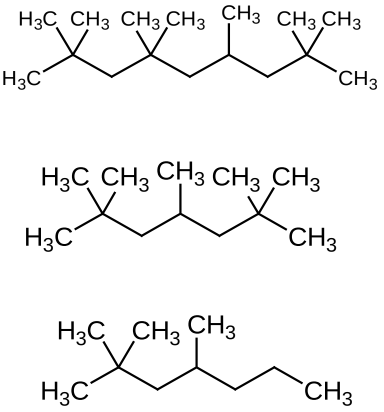
Alcohols



Ketones



Polymer fragments



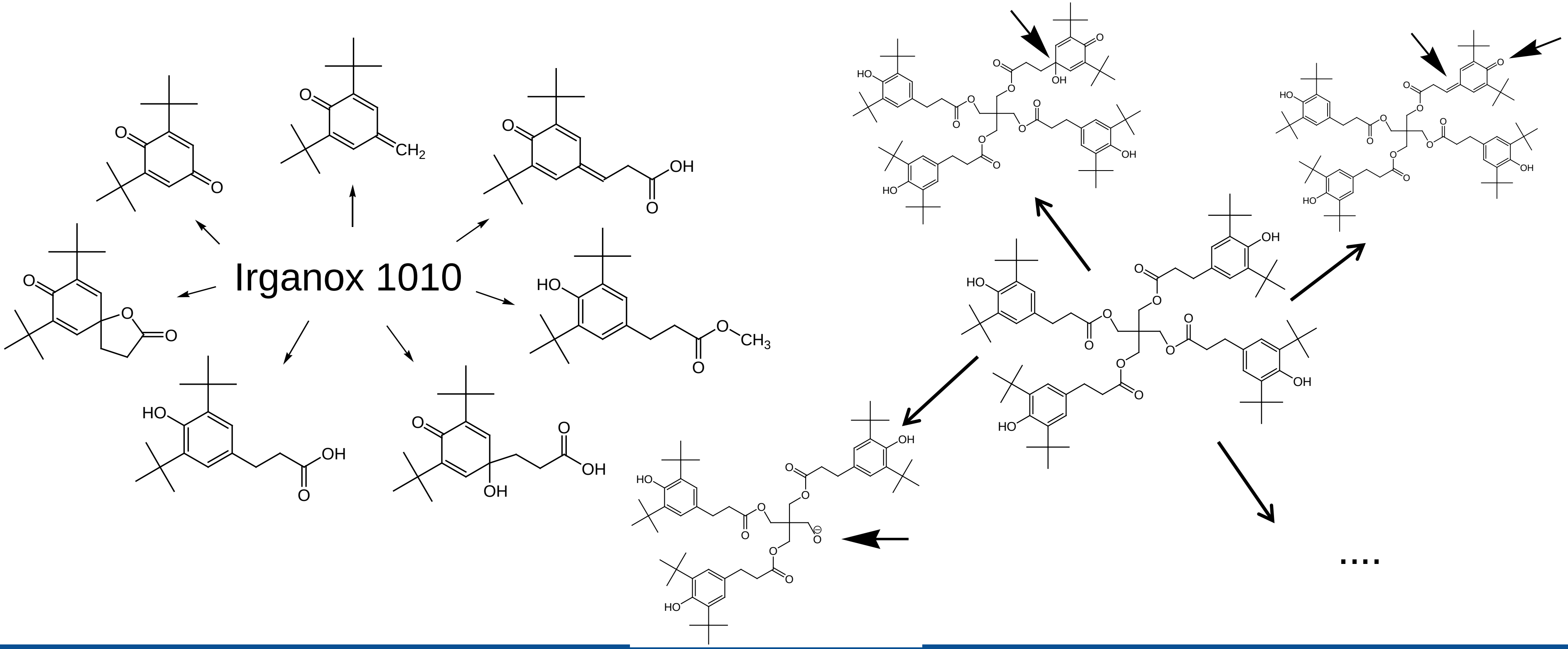
# 4. Composition of Commercial Polymers

## Polymer additive degradation compounds:

Example of polymer additive degradation compounds from **Irganox 1010**

SMALL degradation Compounds

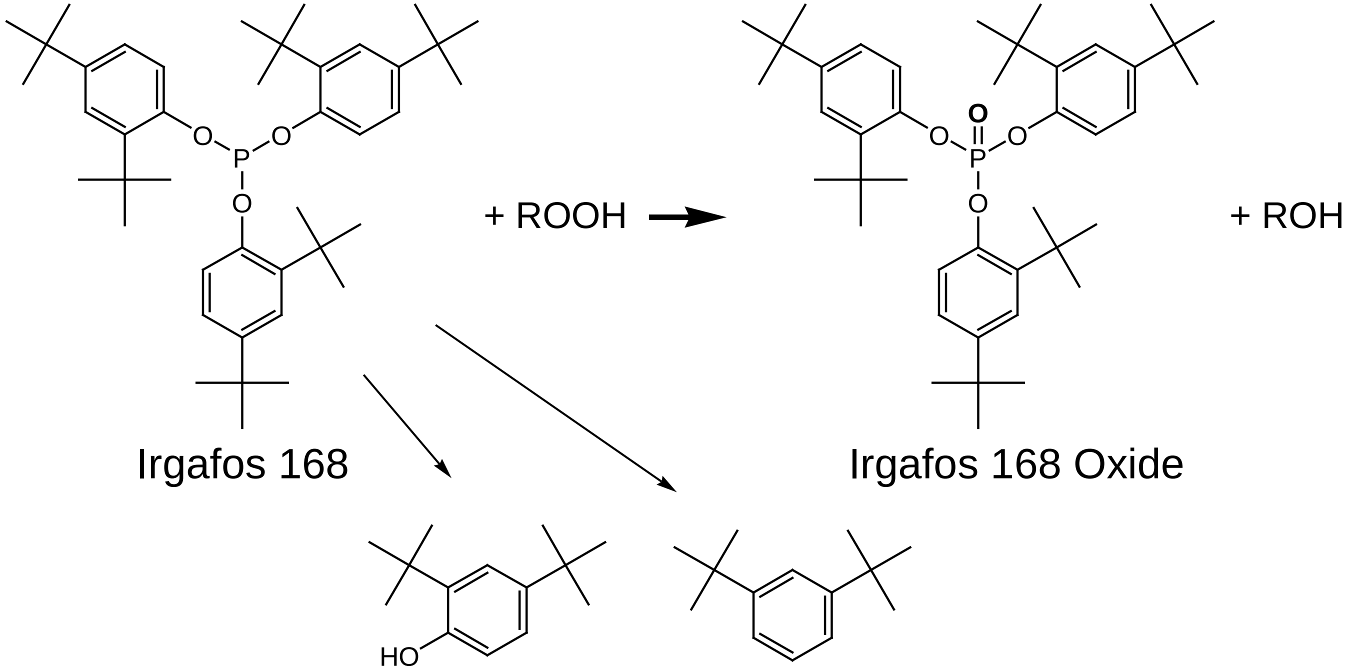
LARGE degradation Compounds



# 4. Composition of Commercial Polymers

## Polymer additive degradation compounds

Example of polymer additive degradation compounds from **Irgafos 168**



Irgafos 168

Irgafos 168 Oxide

*(Remark: also other degradation compounds for Irgafos 168 are known)*

| Name(s) | Formula | Monomer | Examples of Uses |
|---|---|---|---|
| **Polyethylene**<br>low density (LDPE) | $–(CH_2\text{-}CH_2)_n–$ | ethylene<br>$CH_2=CH_2$ | Films for bags, multilayer contact film |
| **Polyethylene**<br>high density (HDPE) | $–(CH_2\text{-}CH_2)_n–$ | ethylene<br>$CH_2=CH_2$ | Bottles, caps |
| **Polypropylene**<br>(PP) different grades | $–[CH_2\text{-}CH(CH_3)]_n–$ | propylene<br>$CH_2=CHCH_3$ | Bottles, caps |
| **Poly(vinyl chloride)** (PVC) | $–(CH_2\text{-}CHCl)_n–$ | vinyl chloride<br>$CH_2=CHCl$ | Bags, tubings |
| **Polystyrene** (PS) | $–[CH_2\text{-}CH(C_6H_5)]_n–$ | styrene<br>$CH_2=CHC_6H_5$ | Secondary packaging |
| **Polytetrafluoroethylene**<br>(PTFE, Teflon) | $–(CF_2\text{-}CF_2)_n–$ | tetrafluoroethylene<br>$CF_2=CF_2$ | Containers, seals, tubes, tubings, “inert” coatings,… |
| **Poly(methyl methacrylate)**<br>(PMMA) | $–[CH_2\text{-}C(CH_3)CO_2CH_3]_n–$ | methyl methacrylate<br>$CH_2=C(CH_3)CO_2CH_3$ | Implantable lenses (IOL) |
| **Poly(vinyl acetate)**<br>(PVAc) | $–(CH_2\text{-}CHOCOCH_3)_n–$ | vinyl acetate<br>$CH_2=CHOCOCH_3$ | Multilayer films |
| **cis-Polyisoprene**<br>natural rubber | $–[CH_2\text{-}CH=C(CH_3)\text{-}CH_2]_n–$ | isoprene<br>$CH_2=CH\text{-}C(CH_3)=CH_2$ | Rubbers |

# THE MECHANISM OF POLYMER MIGRATION

## *A DESCRIPTIVE APPROACH*

# Physics of Leachables Migration from Polymeric Materials

Perhaps **FABES MODEL** could make our lives easier…

**General Formula for Modeling the Migration of Leachables**

$$\frac{m_{F(t)}}{A} = 0.1\, c_{p,0}\, \rho_p\, d_p \left(\frac{\alpha}{\alpha+1}\right)\left[1 - \sum_{n=1}^{\infty} \frac{2\alpha\,(1+\alpha)}{1+\alpha+\alpha^2\, q_n{}^2}\, exp\left(-D_p\, t\, \frac{q_n{}^2}{dp^2}\right)\right]$$

**OOPS… not that easy after all!**

# Leaching Will Depend Upon:

1. **Solubility** of LEACHABLE IN Polymer
2. **Diffusion** of LEACHABLE THROUGH Polymer

# Solubility of LEACHABLE IN Polymer

Is Impacted By

A. **Polymer Morphology**

B. **Temperature**

C. **Age/Sterilization**

D. **Structure & Molecular Weight of LEACHABLE**

# Solubility of LEACHABLE IN Polymer

Is Impacted By

A. **Polymer Morphology**

B. **Temperature**

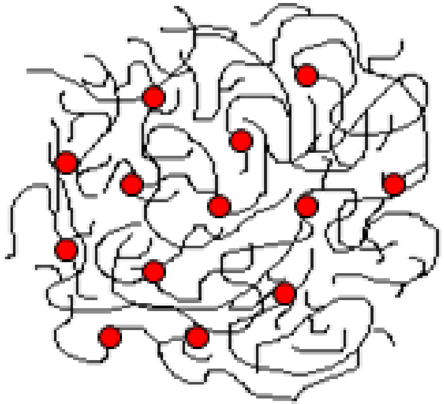
C. **Age/Sterilization**

D. **Structure & Molecular Weight of LEACHABLE**

# Solubility of LEACHABLE IN Polymer

## A. POLYMER MORPHOLOGY

**AMORPHOUS**



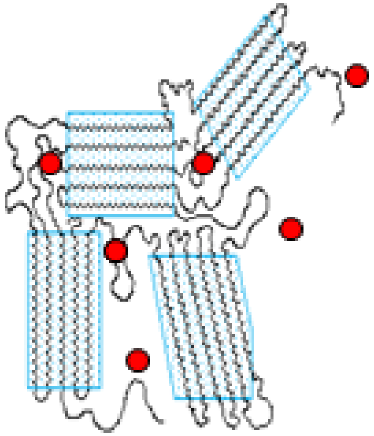
PC, PVC,
PS, PU

**Polymer Additive/Impurity**

- » Dissolves in Amorphous Phase
- » Insoluble in Crystalline Phase

CRYSTALLINE SITES:
BARRIER FOR MIGRATION

**SEMI-CRYSTALLINE**



PE, PP, PET,
EVA, PEEK, PA

# Solubility of LEACHABLE IN Polymer

Is Impacted By

A. **Polymer Morphology**

B. **Temperature**

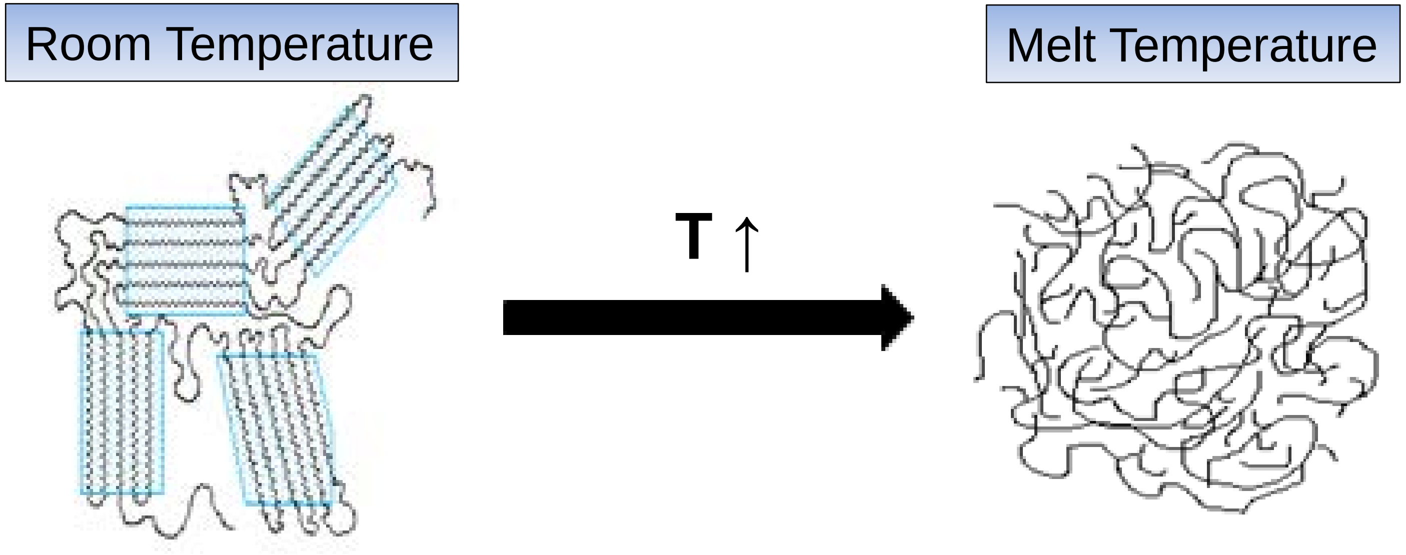
C. **Age/Sterilization**

D. **Structure & Molecular Weight of LEACHABLE**

# Solubility of LEACHABLE IN Polymer

## B. TEMPERATURE

### As Temperature Increase, Solubility Increases



Room Temperature

T ↑

Melt Temperature

RESULT: **BETTER SOLUBILITY** at higher T

**LESS** “CRYSTAL **BARRIER**” FOR MIGRATION

# Solubility of LEACHABLE IN Polymer

Is Impacted By

**A. Polymer Morphology**

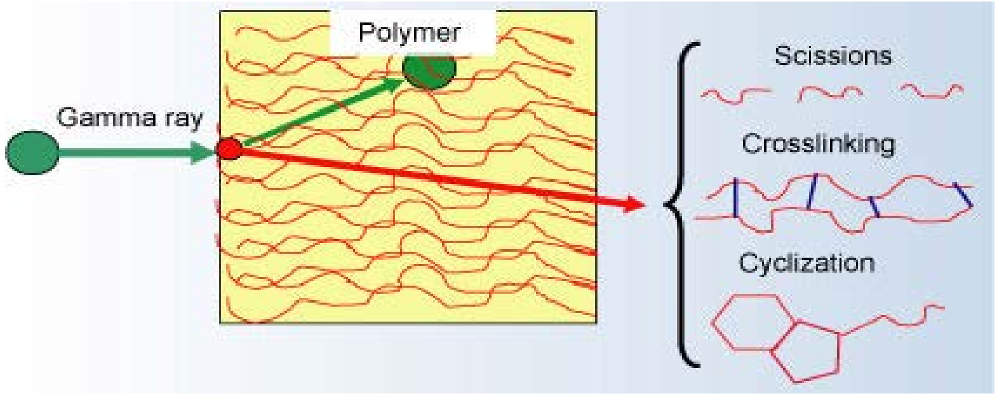
**B. Temperature**

**C. Ageing/Sterilization**

**D. Structure & Molecular Weight of LEACHABLE**

# Solubility of LEACHABLE IN Polymer

## C. AGEING/STERILIZATION



- **Polymer Degradation**
- **Polymer Additive Degradation**
- **Changes in Polymer Crystallinity**

This will **impact** the: LEACHABLES **SOLUBILITY**
LEACHABLES **MIGRATION**

**CONCLUSION:**

» **Perform E&L Testing on Final STERILIZED SYSTEMS**

# Solubility of LEACHABLE IN Polymer

Is Impacted By

A. **Polymer Morphology**

B. **Temperature**

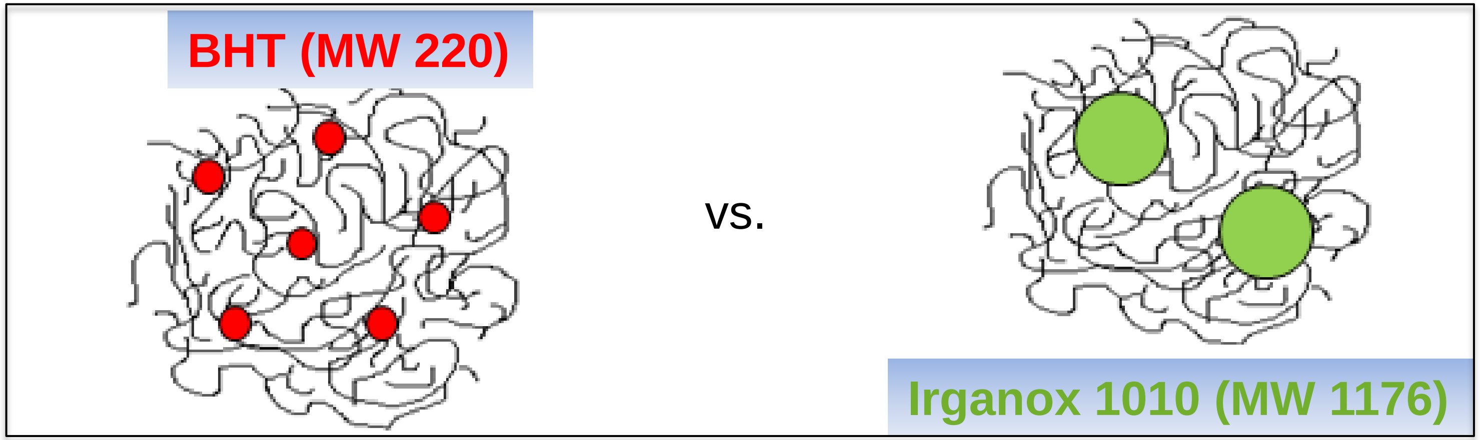
C. **Age/Sterilization**

D. **Structure & Molecular Weight of LEACHABLE**

# Solubility of LEACHABLE IN Polymer

## D. Structure & Molecular Weight of LEACHABLE

» **Molecular Weight**: Larger Molecules = Lower Solubility



» **Polarity "Match":** Structurally ALIKE

**MELTING POINT**: higher $T_{melt}$ - lower solubility

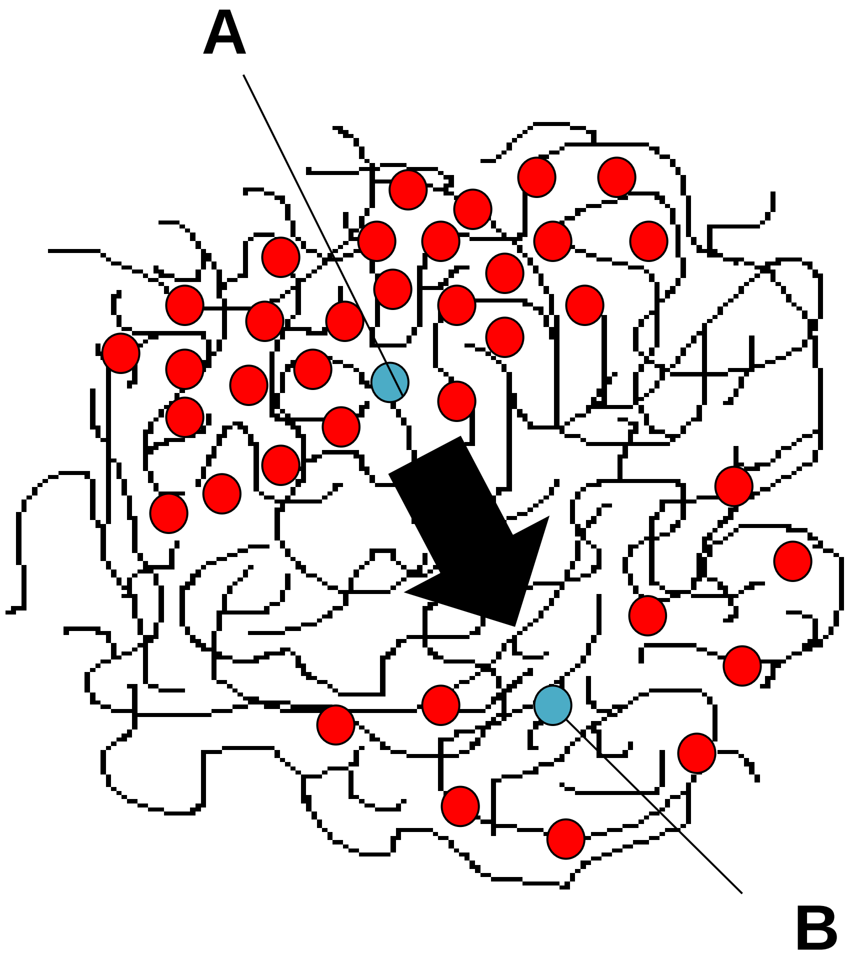
impacted by: - molecular symmetry
- crystallinity

# Leaching Will Depend Upon:

1. **Solubility** of LEACHABLE IN Polymer
2. **Diffusion** of LEACHABLE THROUGH Polymer

# Diffusion of LEACHABLE THROUGH the Polymer

## FICK'S LAW



$$\frac{dC}{dt} = D\,\frac{d^2C}{dx^2}$$

**With D = Diffusion coefficient**

**$D = D_0 \exp(-E/RT)$**

)

# Diffusion of LEACHABLE THROUGH the Polymer

Is Impacted By

A. **Polymer Morphology**

B. **Temperature**

C. **Polymer Type ($T_g$)**

D. **Molecular Weight of LEACHABLE**

E. **Contact Fluid/Environment**

# Diffusion of LEACHABLE THROUGH the Polymer

Is Impacted By

A. **POLYMER MORPHOLOGY**

B. Temperature

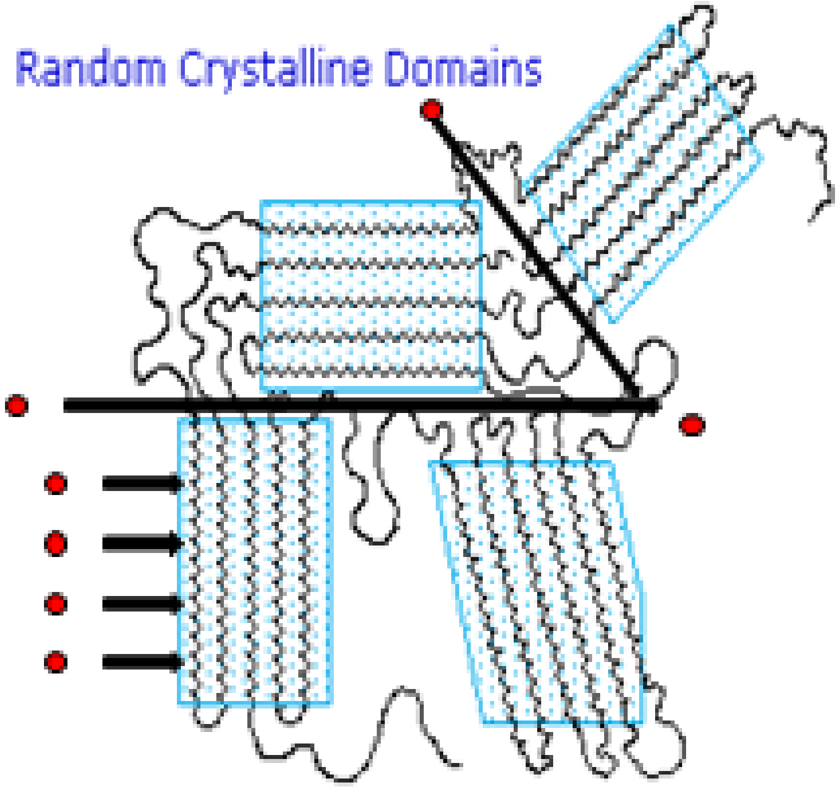
C. Polymer Type ($T_g$)

D. Molecular Weight of LEACHABLE

E. Contact Fluid/Environment

# Diffusion of LEACHABLE THROUGH the Polymer

## A. Polymer Morphology



- **Crystalline Sites:**
  Impermeable Barrier
  for Polymer Additives

- **Filler Particles:**
  Diffusion Barriers for
  Polymer Additives

- **<u>Less Diffusion in</u>:**
  **SEMI-CRYSTALLINE POLYMERS**

# Diffusion of LEACHABLE <u>THROUGH</u> the Polymer

## Is Impacted By

A. Polymer Morphology

**B. TEMPERATURE**

C. Polymer Type ($T_g$)

D. Molecular Weight of LEACHABLE

E. Contact Fluid/Environment

# Diffusion of LEACHABLE THROUGH the Polymer

## B. Temperature

**Remember:**

$$D = D_0 \, e^{(-E/RT)}$$

**Therefore:**

**If T ↑, then D ↑**

**DIFFUSION** of impurities/polymer additives will **Increase Exponentially** when **Temperature Increases**

# Diffusion of LEACHABLE THROUGH the Polymer

Is Impacted By

A. Polymer Morphology

B. Temperature

C. **POLYMER TYPE ($T_g$)**

D. Molecular Weight of LEACHABLE

E. Contact Fluid/Environment

# Diffusion of LEACHABLE THROUGH the Polymer

## C. Polymer Type

### Glass Transition Temperature ($T_g$)

Polymer transitions from **GLASSY** ($t < T_g$)
to **RUBBERY** ($t > T_g$)

**EXAMPLES**

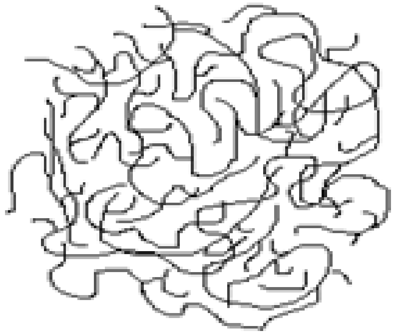
**LDPE $T_g$ = -125 ºC**
**POM $T_g$ = -50 ºC**
**PP $T_g$ = -25 ºC**

**PBT $T_g$ = 70 ºC**
**PVC $T_g$ = 81 ºC**
**ABS $T_g$ = 110 ºC**
**PC $T_g$ = 150 ºC**

**DIFFUSION IN APOLAR > DIFFUSION POLAR POLYMERS**

# Diffusion of LEACHABLE THROUGH the Polymer

## C. Polymer Type



### FREE VOLUME

Ratio of:

$$\frac{\text{Interstitial space (between polymer chains)}}{\text{Total Volume of the Polymer}}$$

Polymers in a **Rubber State** ($T_g < t$)

Typically have **HIGHER** Free Volume

**More Free Volume PROMOTES Diffusion**

# Diffusion of LEACHABLE THROUGH the Polymer

## Is Impacted By

A. Polymer Morphology

B. Temperature

C. Polymer type ($T_g$)

**D. MOLECULAR WEIGHT OF THE LEACHABLE**

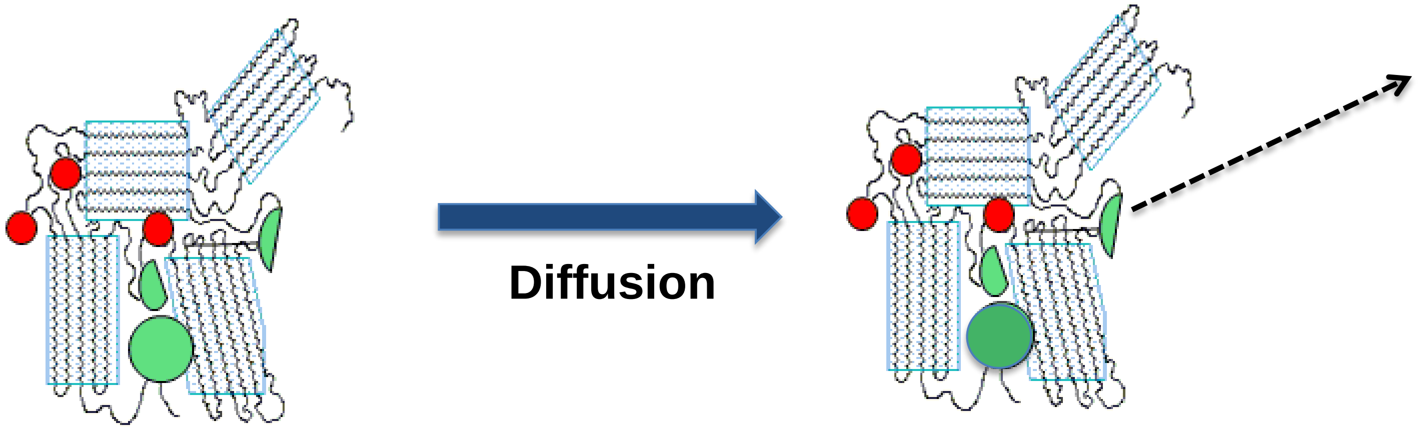
E. Contact Fluid/Environment

# Diffusion of LEACHABLE THROUGH the Polymer

## D. Molecular Weight of LEACHABLE

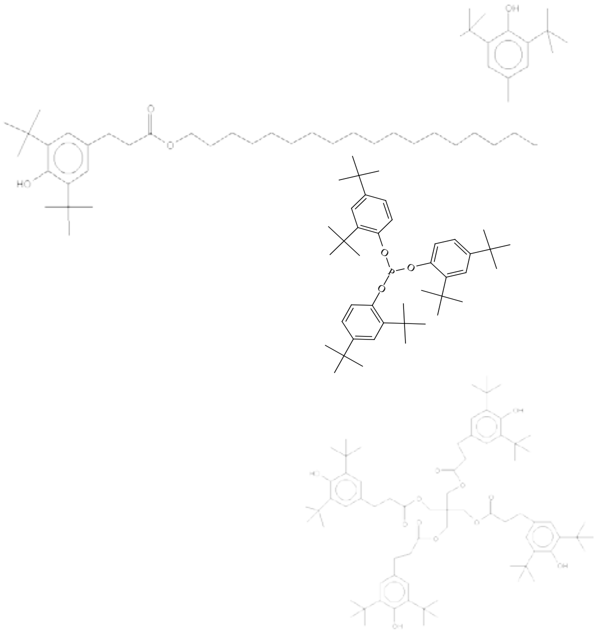
### Diffusion Increases with Decrease in M.W.

- 🔴 BHT (MW 220)
- 🟢 Irganox 1010 (MW 1176)
- ☽ Irganox 1010 degradation compounds (MW 150-300)



# Diffusion of LEACHABLE THROUGH the Polymer

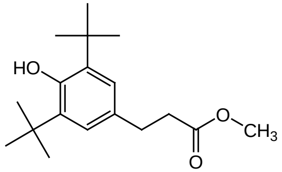
OLIGOMERIC ADDITIVES → REDUCING DIFFUSION



| | | |
|---|---|---|
| BHT: | M.W. 220: | HIGH DIFFUSION |
| Irganox 1076: | M.W. 530 | |
| Irgafos 168: | M.W. 646 | |
| Irganox 1010: | M.W. 1176: | LOW DIFFUSION |

Polymer Additive DEGRADATION INTO SMALLER MOLECULES → FASTER DIFFUSION OF DEGRADANTS

Example:



3,5-Di-*tert*-butyl-4-hydroxyphenyl propionic acid methyl ester

*Degradation product of Irganox 1010 / Irganox 1076*

# Diffusion of LEACHABLE THROUGH the Polymer

## Is Impacted By

A. Polymer Morphology

B. Temperature

C. Polymer type ($T_g$)

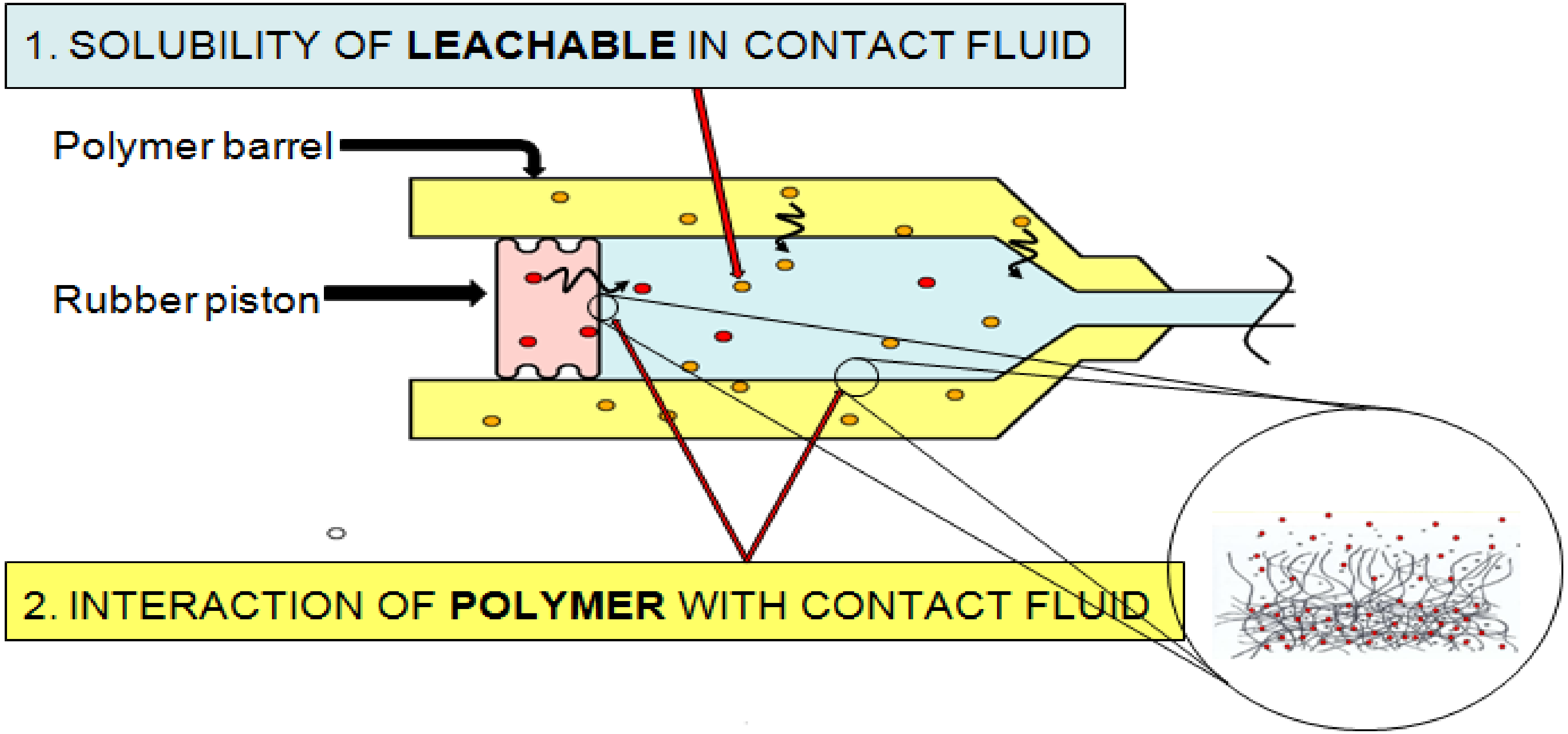
D. Molecular Weight of the Leachable

**E. CONTACT FLUID/ENVIRONMENT**

# Diffusion of LEACHABLE THROUGH the Polymer

## E. Contact Fluid/Environment

### Two Important Aspects

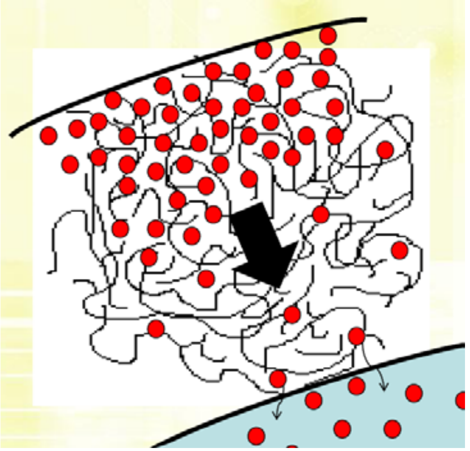


1. SOLUBILITY OF **LEACHABLE** IN CONTACT FLUID

2. INTERACTION OF **POLYMER** WITH CONTACT FLUID

# **Diffusion of LEACHABLE THROUGH the Polymer**

## 1. INTERACTION CONTACT FLUID - LEACHABLE



IN GENERAL:

*For most Organic Compounds:*

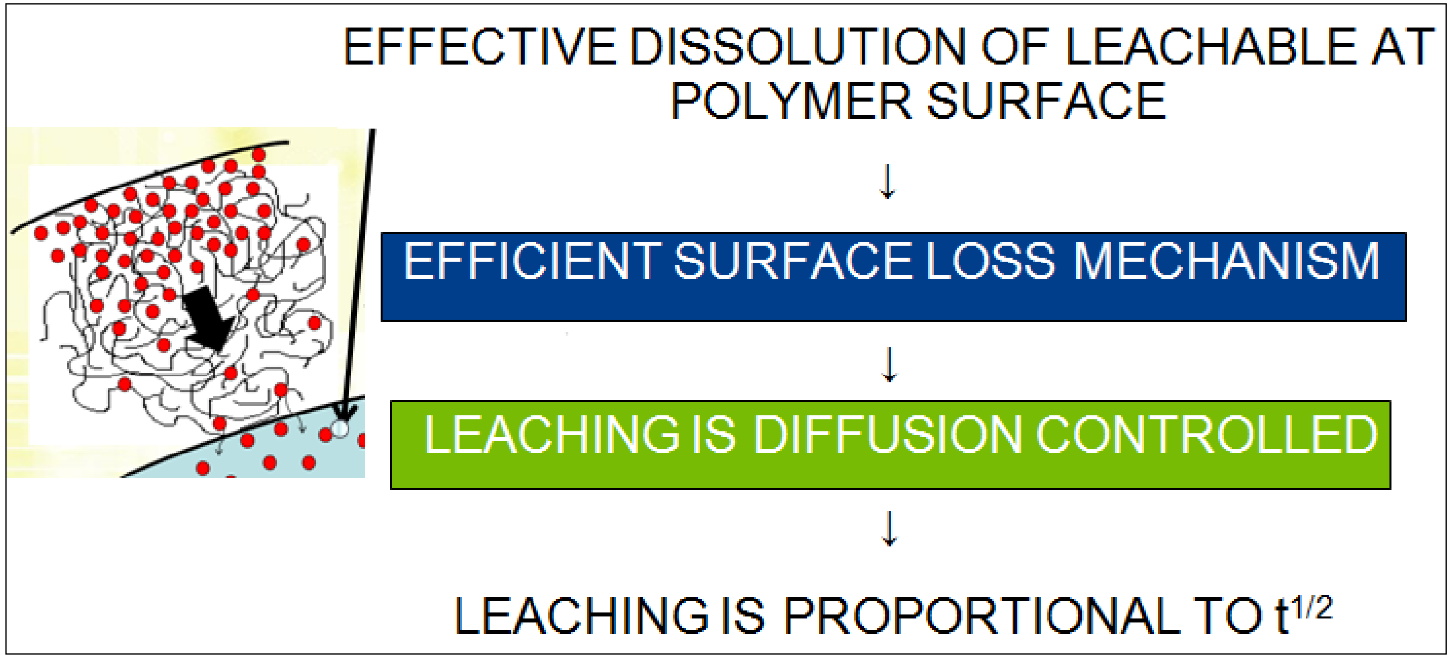
**ORGANIC**/HYDROPHOBIC CONTACT FLUIDS = **HIGH SOLUBILITY** SOLVENTS

WFI/**HYDROPHILIC** CONTACT FLUIDS = **LOW SOLUBILITY** SOLVENTS

# Diffusion of LEACHABLE THROUGH the Polymer

## E. Contact Fluid/Environment

### 1. Solubility of the Leachable in the Contact Fluid



EFFECTIVE DISSOLUTION OF LEACHABLE AT POLYMER SURFACE

↓

EFFICIENT SURFACE LOSS MECHANISM

↓

LEACHING IS DIFFUSION CONTROLLED

↓

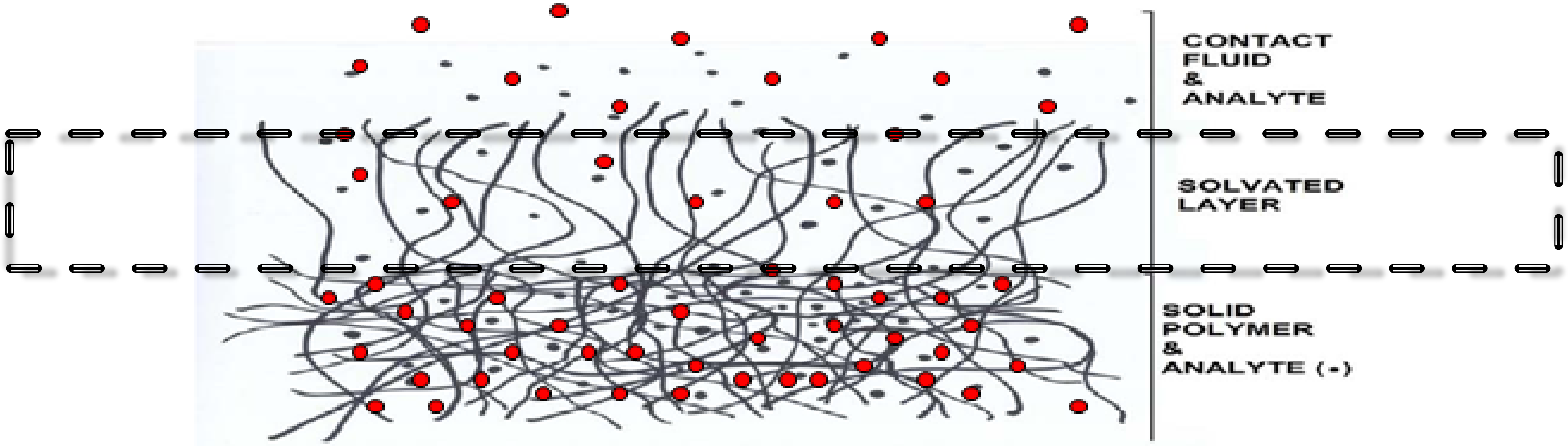
LEACHING IS PROPORTIONAL TO $t^{1/2}$

# Diffusion of LEACHABLE THROUGH the Polymer

## E. Contact Fluid/Environment

### 2. Interaction of the Contact Fluid with the Polymer

SOLVENT CAN "PLASTICIZE" or "SWELL" POLYMER:
**SOLVATED LAYER**

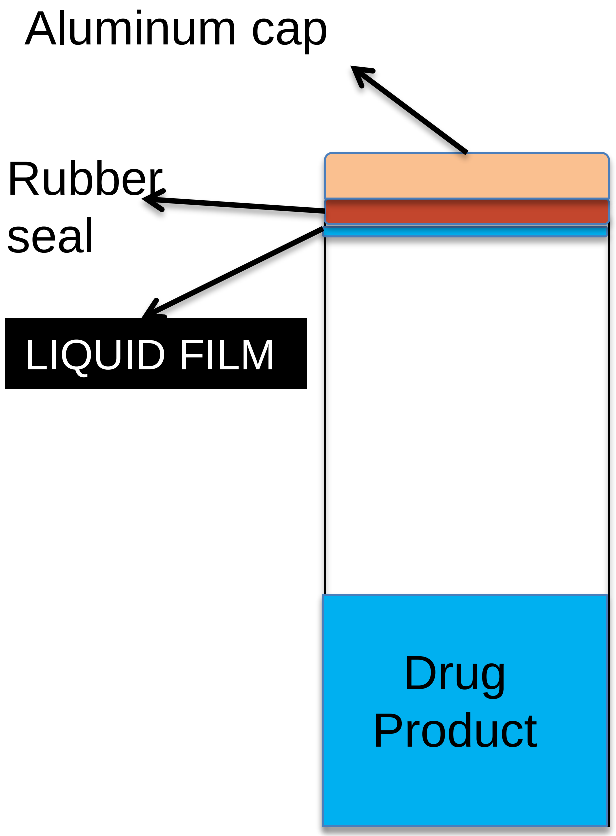


ENHANCED DIFFUSION OF LEACHABLES
↓
ACCELERATED LOSS

# Application Specific Effects

1. **SuperSaturation**
2. **Outgassing**
3. **Blooming**

# SUPERSATURATION



**LIQUID FILM** is formed via

- Evaporation during storage
- Transportation

**Film** may be different in composition than the DP

**Diffusion** of Rubber Compounds into small volume

- Metals
- Organic

Can cause **Aggregation, Particle Formation**

May be **irreversible**

- Particles do not dissolve anymore when in contact with the total DP volume

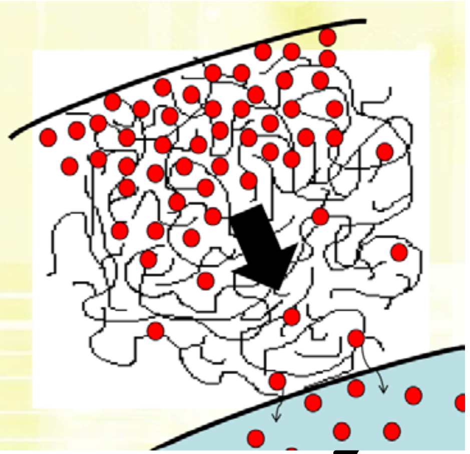
**LIQUID FILM** may also act as **"barrier"**

- for migration
- for outgassing (see next slide)

# OUTGASSING

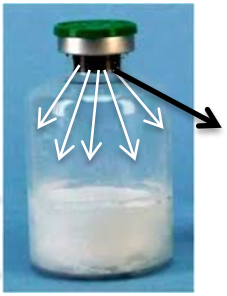
Material (e.g.):
Film *(Overwrap)*

Rubber
*(Lyo Vial,
Needle Shield)*



Solvent: air, nitrogen, gas phase

No “Liquid Film” barrier
on rubber
*(see previous slide)*



OUTGASSING of
RUBBER CLOSURE

Lyo Cake
= adsorbent

*High Suface Area and extremely Dry*

Outgassing is mainly an issue for:

- Volatile Organic Compounds
- Semi-Volatile Organic Compounds

# BLOOMING

**What is it?**

- Blooming is a physical phenomenon
- Observed in polymers which are (super)saturated with additives
- A process of diffusion controlled migration of additives from the polymer
- Typical for additives with low solubility & high diffusion rate

**Typical Conditions when blooming occurs**

- » Low solubility of the additive in the polymer
- » High diffusion of the additive through the polymer
- » Dosing of the additive into the polymer close to the solubility of the additive in polymer
- » Low temperature applications may accelerate blooming process (lower solubility, *but also lower diffusion...*)