THE MECHANISM OF POLYMER MIGRATION
A DESCRIPTIVE APPROACH

PDA WORKSHOP
EXTRACTABLES – LEACHABLES
Rome
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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!

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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

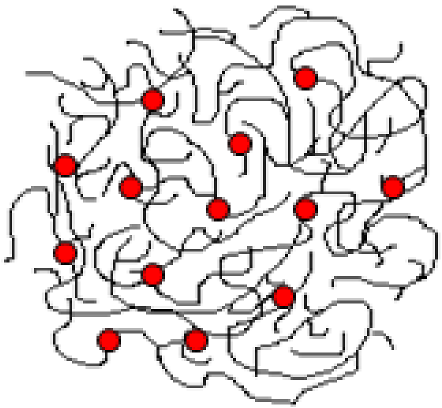
C. Age/Sterilization

D. Structure & Molecular Weight of LEACHABLE

Solubility of LEACHABLE IN Polymer

A. POLYMER MORPHOLOGY

AMORPHOUS



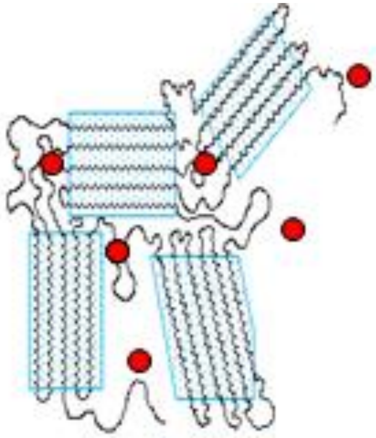
PC, PVC, PS, PU

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

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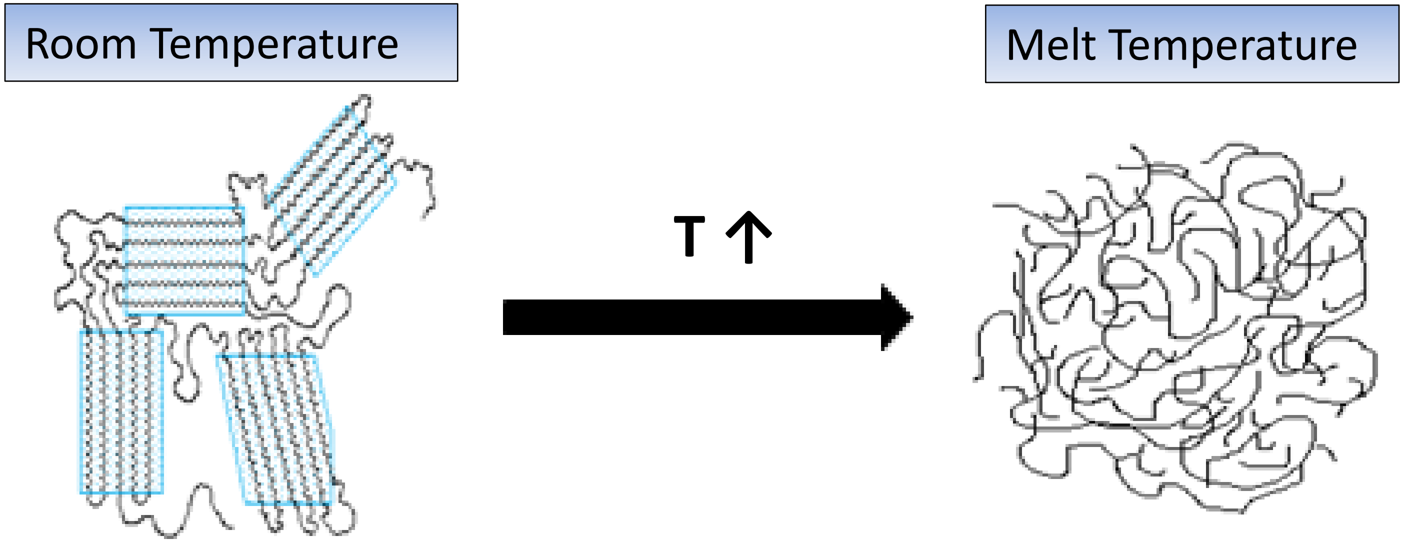
Solubility of LEACHABLE IN Polymer

B. TEMPERATURE

As Temperature Increase, Solubility Increases



RESULT: **BETTER SOLUBILITY** at higher T

LESS "CRYSTAL **BARRIER**" FOR MIGRATION

Solubility of LEACHABLE IN Polymer

Is impacted by

A. Polymer Morphology

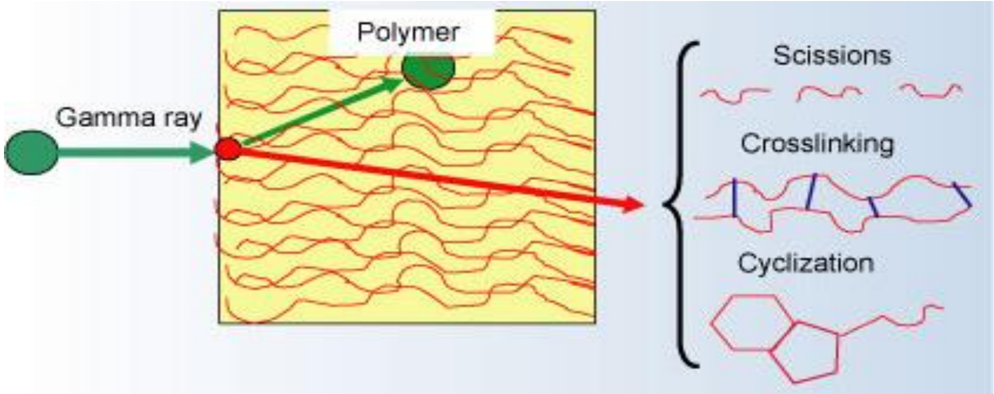
B. Temperature

C. **AGE/STERILIZATION**

D. Structure & Molecular Weight of LEACHABLE

Solubility of LEACHABLE IN Polymer

C. AGE/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**

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Solubility of LEACHABLE IN Polymer

Is Impacted By

A. Polymer Morphology

B. Temperature

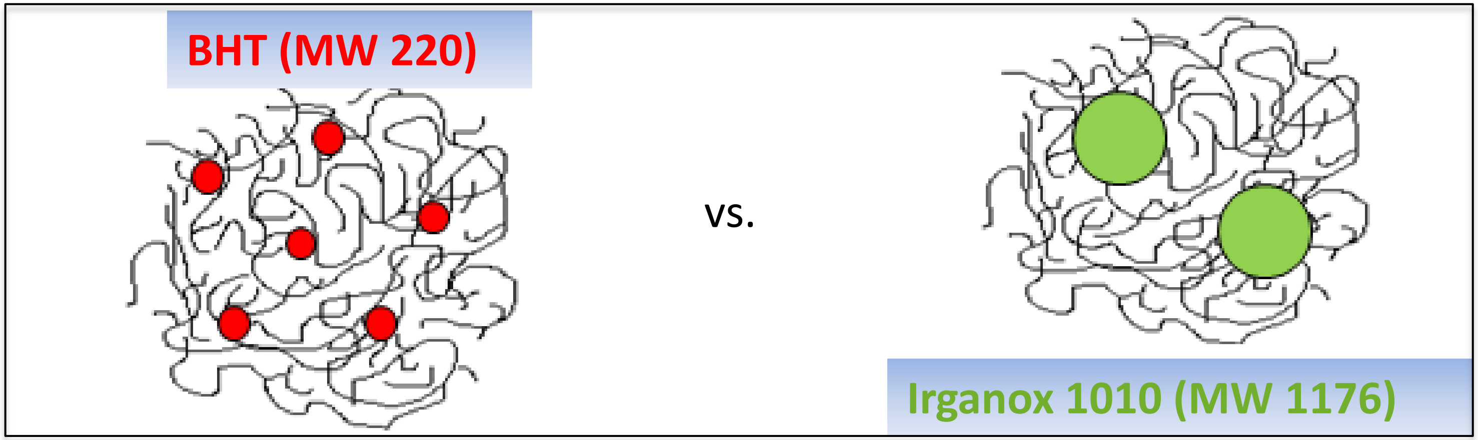
C. Age/Sterilization

D. STRUCTURE & MOLECUALR 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

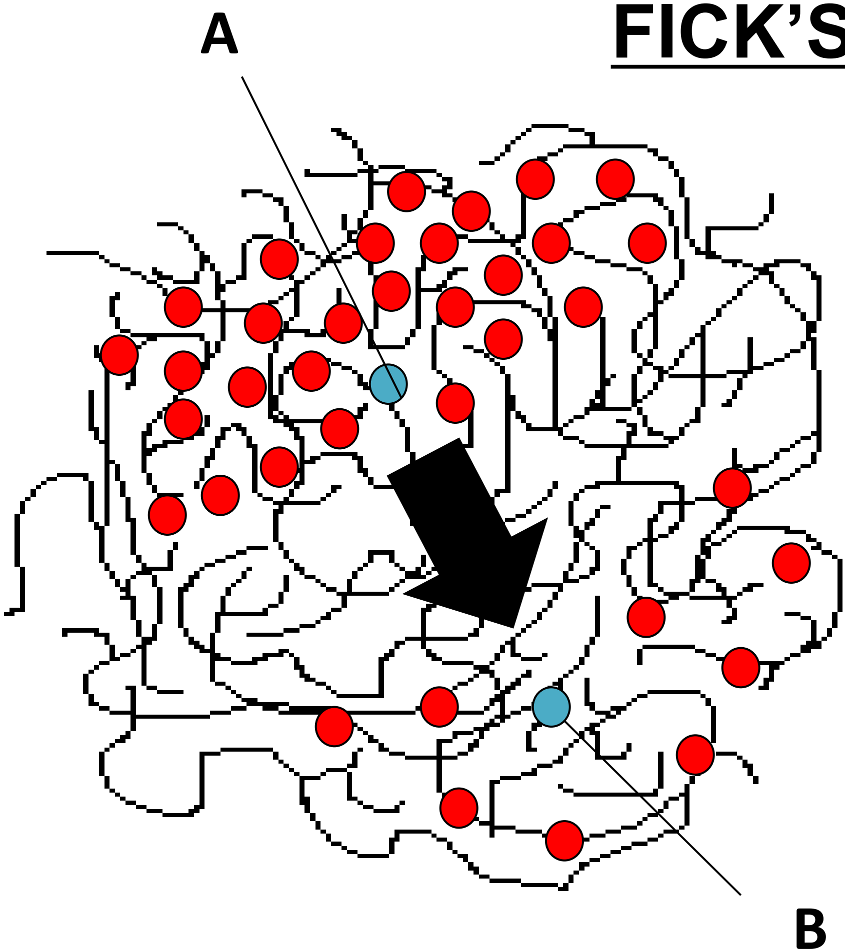
Leaching Will Depend Upon:

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**

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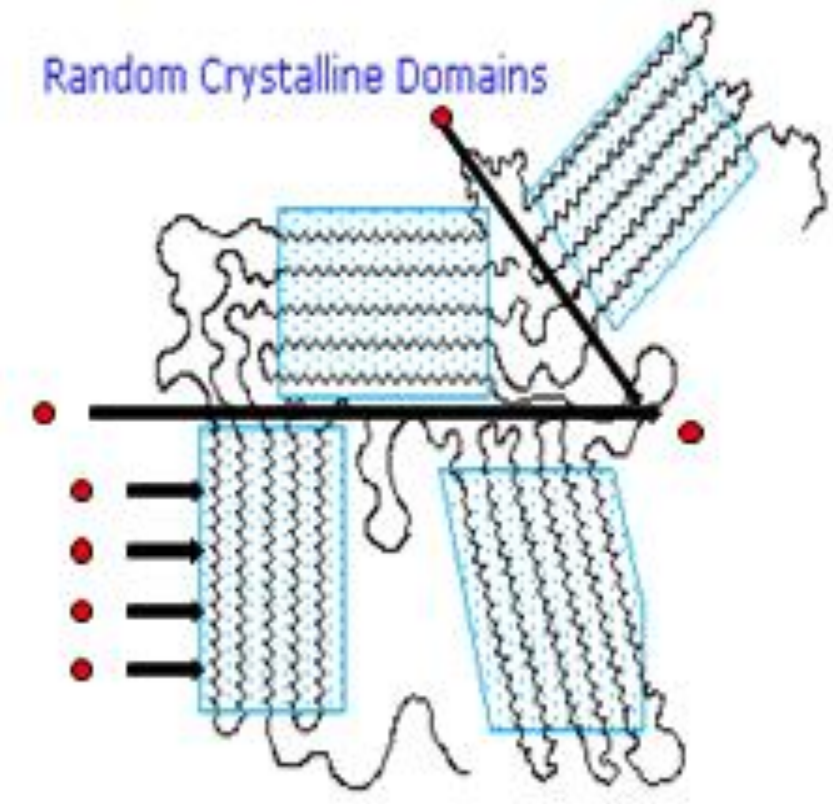
Diffusion of LEACHABLE THROUGH the Polymer

Is Impacted By

A. **POLYMER MORPHOLOGY**
B. Temperature
C. Polymer Type (T_g)
D. Molecular Weight of LEACHABLE
E. Contact Fluid/Environment

A. Polymer Morphology



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

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

- **Less Diffusion in:**
  SEMI-CRYSTALLINE POLYMERS

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

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

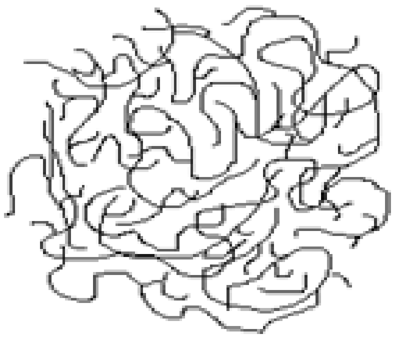
Glass Transition Temperature (T_g)

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

EXAMPLES

LDPE	T_g = -125 ºC	**PBT**	T_g = 70 ºC
POM	T_g = -50 ºC	**PVC**	T_g = 81 ºC
PP	T_g = -25 ºC	**ABS**	T_g = 110 ºC
		PC	T_g = 150 ºC

DIFFUSION IN APOLAR > DIFFUSION POLAR POLYMERS



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 LEACHABLE

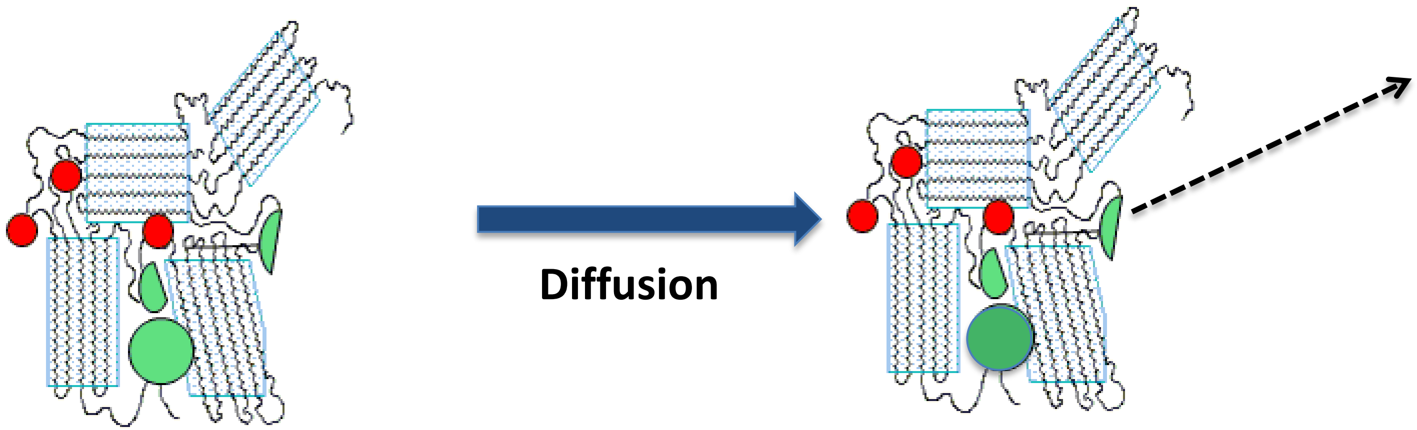
E. Contact Fluid/Environment

Diffusion of LEACHABLE THROUGH the Polymer

D. Molecular Weight of LEACHABLE

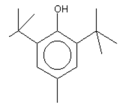
Diffusion Increases with Decrease in M.W.

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

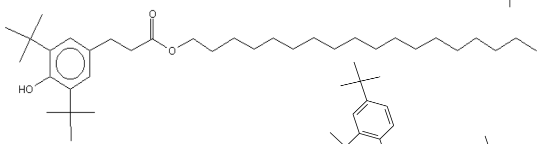


Diffusion of LEACHABLE THROUGH the Polymer

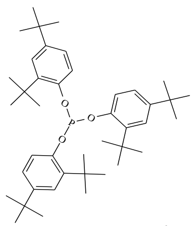
OLIGOMERIC ADDITIVES → REDUCING DIFFUSION



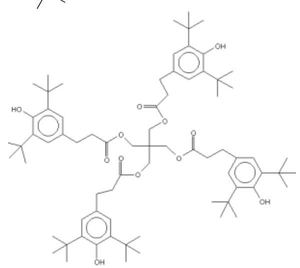
BHT: M.W. 220: HIGH DIFFUSION



Irganox 1076: M.W. 530



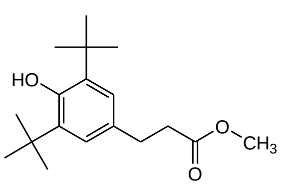
Irgafos 168: M.W. 646



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 LEACHABLE

E. CONTACT FLUID/ENVIRONMENT

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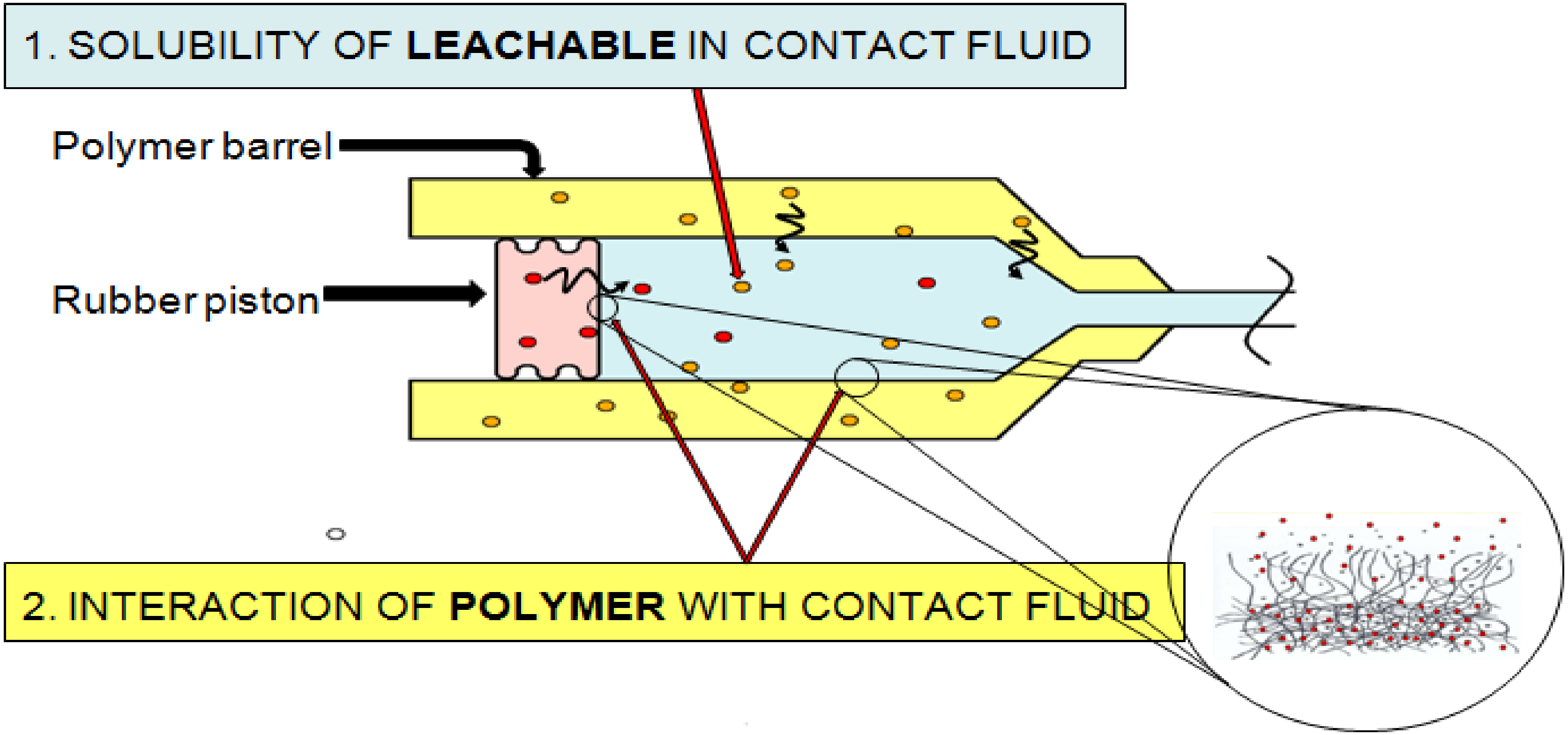
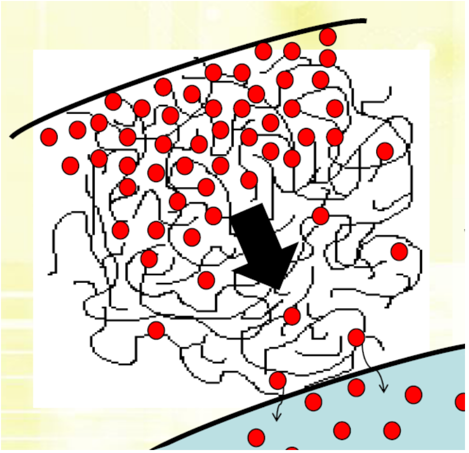
E. Contact Fluid/Environment

Two Important Aspects



E. CONTACT FLUID

1. INTERACTION CONTACT FLUID - LEACHABLE



IN GENERAL:

For most Organic Compounds:

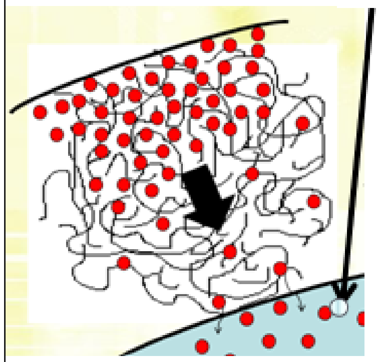
ORGANIC/HYDROPHOBIC CONTACT FLUIDS = **HIGH SOLUBILITY** SOLVENTS

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

Diffusion of LEACHABLE <u>THROUGH</u> 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

↓

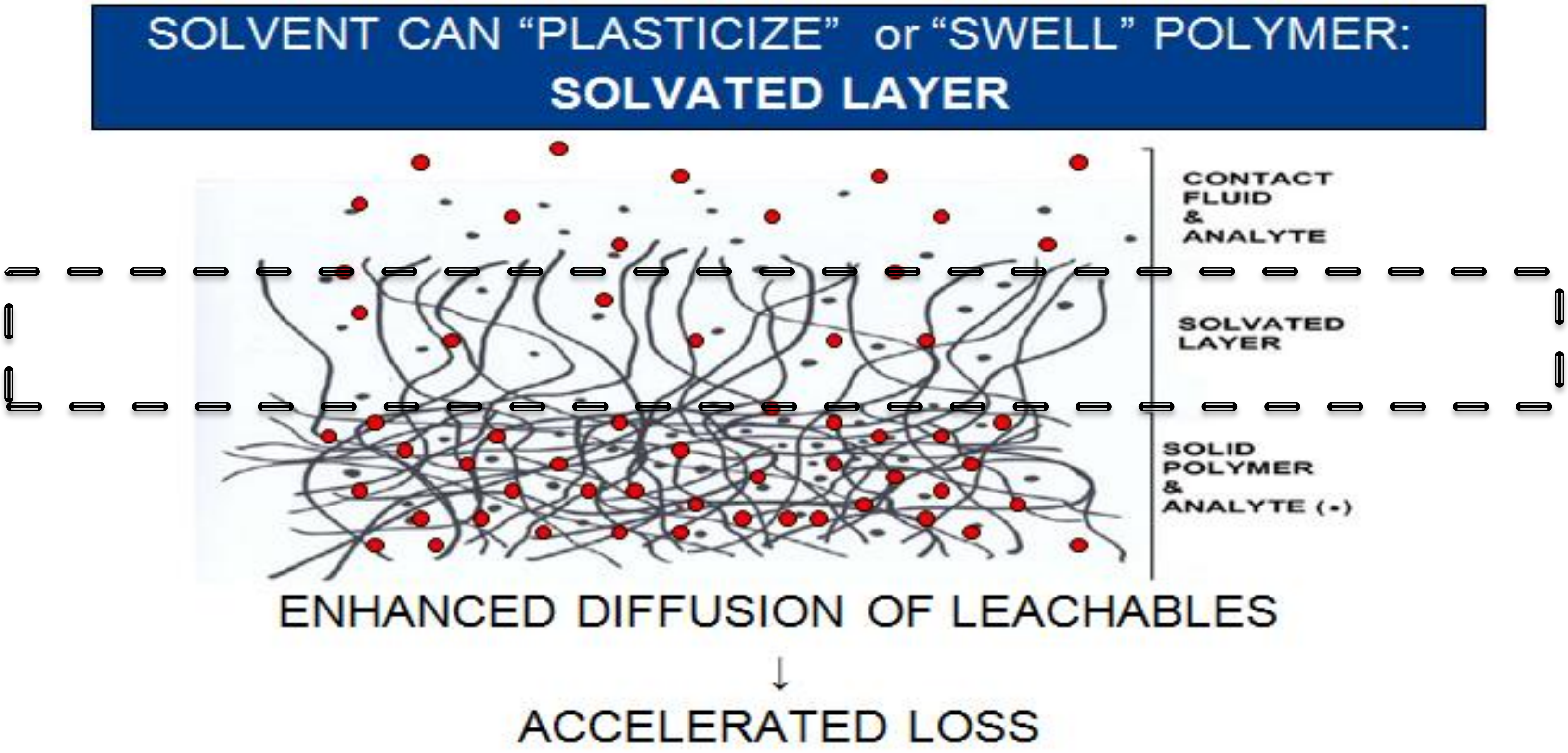
LEACHING IS DIFFUSION CONTROLLED

↓

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

E. Contact Fluid/Environment

2. Interaction of the Contact Fluid with the Polymer



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Application Specific Effects

1. Super Saturation
2. Outgassing
3. Blooming

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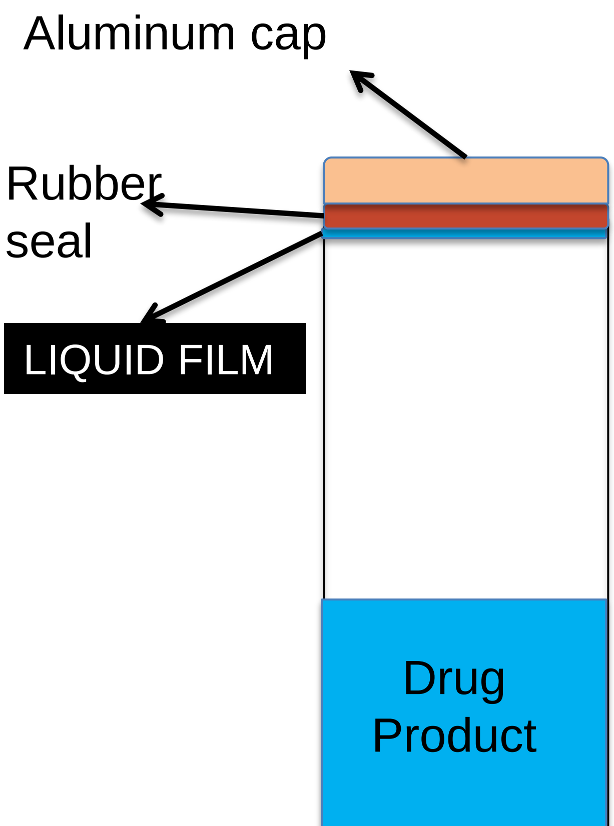
SUPERSATURATION



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**

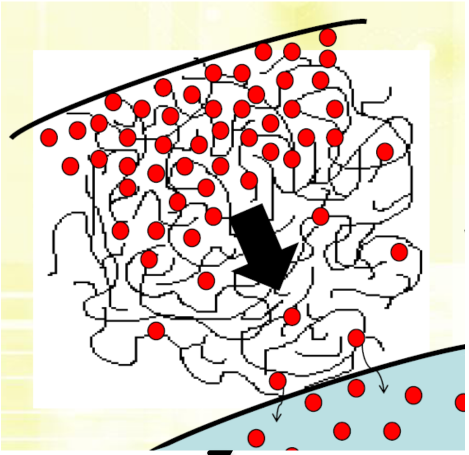
May be **irriversible**
- Particles do not dissolve anymore when in contact with the total DP volume

LIQUID FILM may also act as **"<u>barrier</u>"**
- for migration
- for outgassing (see next slide)

OUTGASSING

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

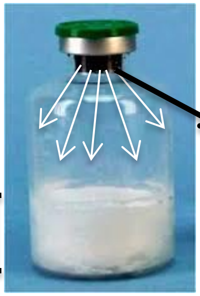
Rubber
(Lyo Vial,
Needle Shield)



Solvent: air, gas phase

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

Lyo Cake
= adsorbent



OUTGASSING of
RUBBER CLOSURE

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...*)

LUNCH TIME ;-)

…finally!