Process for low migration qualification in the food, pharma and medical industry

Definition of migration, set-off, low migration inks and the printing process

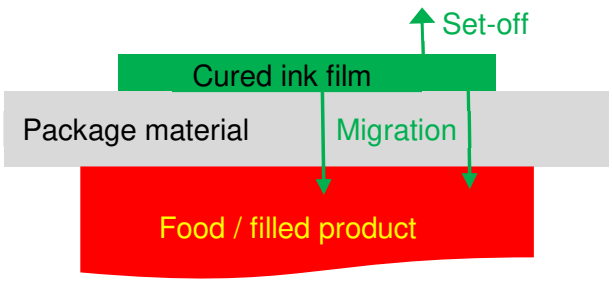
Migration substances can modify products, its odor, active substance intensity of a pharma product, and taste. They can be unhealthy. To understand migration, let us begin by differentiating between migration and set-off, and then define low-migration.

Migration

Migration is the diffusion of the remaining ingredients of the cured ink film through the packaging material into the filling product.

Set-off

Set-off, is the transfer of remaining ink substances from the printed surface of a packaging substrate to its unprinted, product-contact surface. Set-off occurs when the two surfaces come into contact, i.e. when the substrate material has been stacked or wound onto rolls. In general, set-off is not visible, as only molecules of the ink substances are transferred.



The diffusion of cured ink substances needs time, and is temperature related. Stable results on diffused ink substances can be expected after several days or also after a longer time period related to the shelf life of a product.

Reasons for migration:

- Residue of monomers
- Photoinitiators
- Decomposition product of photoinitiators
- Ink additives
- Incomplete curing

In a heavy set-off situation also normally non-migrating pigments and binders may transfer to the filling product.

There are “quick and dirty” methods for testing for possible ink migration, which can be made within minutes of printing. But these methods are no guarantee for low migration.

One, a detectable and distinct “print” smell is an indication of migration. Two, when an ethanol-soaked paper towel is wiped across the print and the towel shows ink residue (the ink’s color), then there is the probability of improperly cured inks and a high risk of set-off and/or migration.

Low migration inks

UV DoD inks have ingredients smaller than 1000 Da ($1.66 \cdot 10^{-21}$ g) →1000g/mol molecular weight and for that reason these inks can migrate.

Only ingredients listed as positive are used, and in defined volumes, the legal values of which fall below the “worst case” migration limits.

Low migration inks are formulated in a defined and monitored process so to not exceed the legal limits for migration.

Printing process

In the printing process with UV DoD inks we have to take care of the following information:

- Packaging material and thickness
- Layer thickness of the cured ink
- Curing energy (Intensity by time, Joule); be aware that Intensity by time is not constant → the crease of UV power is not equal to the reduction of exposure time and vis versa

Low migration can be achieved only by properly monitored and qualified process steps.

Legislation

In the food, pharma, and medical industries, although only the owner of the brand is responsible for packaging regulation compliance, all members of the packaging supply chain must exchange relevant information up and downstream.

Packaging in the food, pharma, and medical industries is highly regulated. Several guidelines and laws must be adhered to.

Most important legislation is as follows:

- COMMISSION REGULATION (EC) No 1935/2006
  on materials and articles intended to come in contact with food
- COMMISSION REGULATION (EC) No 2023/2006
  GMP on materials and articles intended to come in contact with food
- COMMISSION REGULATION (EU) No 10/2011
  on materials and articles intended to come in contact with food
- CH BGVO SR 817.023.21
  Swiss ordinance on materials and articles intended to come in contact with food

Migration values

Two factors create “migration value”, The EU-cube model and Specific Migration Limit (SML). The model determines a European’s average daily consumption of food, and the SML determines the maximum limit of packaging material (including ink components) that may transit to the package’s food product.

The EU-cube compromises 6 sides, each with an edge length of 1 dm. The cube is equivalent to a 6 dm^2 surface, and represents 1 kg of food. The EU-cube corresponds to the maximum food consumption of an average, 60 kg EU citizen per day.

According to the regulation “EN10/2011 on plastic materials and articles intended to come into contact with food”, if no lower Specific Migration Limit (SML) values are set, only a maximum of 10 mg/dm^2 of the packaging material may transit to the filling product.

The formula to calculate migration value is as follows::

10 mg/dm^2 = 60 mg/kg = 60 ppm = 60’000 ppb

1 µg/dm^2 = 6 µg/kg = 6 ppb

Migration limits

Food packaged in Switzerland as well imported food packages intended for the Swiss market must comply with “SR 817.023.21 Swiss Ordinance on Commodities”. The following values must be met:

- Maximum 10 ppb for non-evaluated materials (listed in Appendix 6, list B of the CH BGVO SR 817.023.21
- The specified SML value listed in Appendix 6, list A of the CH BGVO SR 817.023.21 or if no SML is declared the value 60 ppb will be valid for these chemicals

For food packages manufactured and sold in the EC (excluding Switzerland) SML for materials listed in EN10/2011 will be valid.

The inks used in the manufacturing of food packages for Nestlé must be compliant with the Nestlé Guidance Note.

According to the (EC) No. 1935/2004 (Art. 3) regulation, materials or articles “intended to come in contact directly or indirectly with food”, must “preclude substances from being transferred to food in quantities large enough to”:

- endanger human health
- bring about an unacceptable change in the food’s composition or
- a deterioration of its organic properties

Simulants for migration testing

According to the regulation 82/711/EEC with its changes in the regulation 97/48/EC and the regulation 85/572/EEC with its last changing regulation 207/19/EG the following simulants are to be used:

Food type	**Simulant**
aqueous foods (ph > 4.5)	distilled water
acidic foods	3% acetic acid
dairy products	50% ethanol
alcoholic products	10% ethanol
fatty food	modified Polyphenylenoxid (MPPO, Tenax®)
	95% ethanol
	Isoctan
	alternative test simulant as a substitute for simulant D (olive oil)
dry food products	According to regulation 97/48/EG dry food products need no simulant.

Packaging systems

In the past, primary and secondary packagings were differentiated. For example, the secondary packaging was a carton box containing a PE bag with flakes inside or a sticker on a PET drink bottle. The primary packaging was then the PE bag and the PET bottle.

Today we no longer differentiate between primary and secondary packaging for food, pharma, and medical products. Crucial is that no diffusion of all packaging materials is transferred to the filling product. This is in contradiction to the regulation (EC) No. 1935/2004 and the CH BGVO SR 817.023.21.

Printing on packaging issues

Some materials will exhibit ink penetration. Yet ink correctly formulated and cured will lower the risk of ink remaining substances penetrating into or through the substrate.

UV energy, wavelength, spectrum, and life time are important curing parameters for ink polymerization. It must be taken into account that E = P * t is not a constant for polymerization. It is a misperception that when the window to UV exposure is small that it is possible to increase the UV power to achieve proper curing, i.e. polymerization. Alternately, it is not possible to achieve proper curing with decreased UV power by enlarging the window of exposure. Minimum time plus minimum power must be accurately calculated to achieve the necessary chemical reaction for proper polymerization.

The smell of the cured ink can be a simple indicator of migration. If the printed surface smells of ink, there is high probability of migration or set-off.

Considerations in the printing process

- What packaging materials will be used?
  Design of the materials
- What is the filled product?
  Dry, water based, alcoholic, fatty, oily
- Special production parameters?
  Autoclaving, hot filling, sealing
- Is a diffusion of the printed packaging to the fill product possible?
  Barrier layer existing between printed packaging material and filling product (glass, minimum 9 µm aluminum foil)

Qualification process for low migration application

Either the qualification process for a low-migration application ends in a certified process, or it fails. To speed up the certification process, developing a step-by-step procedure is a good decision.

The use of ingredients from the Nestlé positive list is a first step to the fulfilment of the application requirements.

The second step is fulfilling an ink formulation dedicated to the parameters of the substrate.

The third step is printing-process defined: pretreatment, printing (layer thickness), pinning, cure delay and curing (achieving high polymerization grade).

If, after following these three steps, the polymerization results in adhesion, scratch, and ambient-conditions resistance, then it can be test for migration in a certified laboratory. The test conditions are defined by the laboratory and the packaging manufacturer.

A statement of composition (SoC) is handed over to the laboratory. This SoC enables the laboratory to search for components in/on the filling product.

A repetition of the steps is necessary if the first migration test fails. But a failed test means that the product responsible for the failure is identifiable and can be substituted, or the formulation or process can be altered in order to produce a positive test result.

GMP (Good Manufacturing Practice)

Area of application

The regulation (EC) No 2023/2006 defines GMP for food-contact materials and articles that are based on the appendix to the regulation (EC) No. 1935/2004. Both materials and articles are required to fulfill the compliance.

Implication

Producers of packaging materials have to implement a quality management and control system. They also have to implement a documentation system to monitor their production, to be made available upon demand of the authority.

Quality management system

The communication in the supply chain is key to fulfilling the requirements of a quality management system.

Some important points of the quality control system:

- The correct and evaluated materials are in use
- The correct and evaluated inks are in use
- The process is qualified and validated (pretreatment, printing, pinning, cure delay, curing)
- Skilled employees are running the processes

The supplier has to install an effective and documented quality control system and has to follow its application. The quality control system has to be in line with the customer's needs.

Who is affected by GMP

Every company in the supply chain is affected by the quality management and control system (GMP). All production processes have to be in line with GMP.

Each supplier can take responsibility for its process only:

Packaging supplier	- inks are optimized for the specified application
Ink supplier	- inks are optimized for the specified application
Printer	- the print process is qualified and validated
Filler of goods	- qualified and validated packaging material is in use
Brand owner	- the finished goods are in line with the regulation (EC) No. 1935/2004

Conclusion

Migration or set-off

Do we expect migration or set-off (stacks or rolls) in our printing process?

Kind of migration test

What migration test do we expect (simulants)?

Legislation

Do we know the regulation for low migration applications?

Packaging

Is the packaging material defined? Do we know the design of it?

Ink technology

Do we the ink technology and is it following guidelines for low migration?

Printing process

Do we know our printing process? Can we validate our printing process (pretreatment, layer thickness, curing)

Quality management system

Do we have a quality management system to fulfill GMP?

Hapa UV DoD ink series

Aposta®

Standard OEM inks

Enserra®

Low migration OEM inks

Ascepte®

Standard Healthcare inks

Evitar®

Low migration Healthcare inks