Polymeric Gels in Flexible Medical Device Packaging
An SPMC White Paper

Executive Summary ........................................2
The Challenge of Gels ........................................2
Classification of Particulate ..............................2
The Nature of Gels ...........................................3
Definition of Gels .............................................3
Three General Varieties of Gels ......................4
Process Controls Issues .................................5
Gels and Sterile Barrier Issues ......................6
Gels and Lamination .......................................6
Integrity Considerations .................................7
Conclusion .....................................................7
SPMC Technical Group .................................8
EXECUTIVE SUMMARY

This white paper presents background and information regarding gels in flexible medical device packaging, as well as considerations related to the impact of gels on package integrity. We will share technical experience and a data-based approach to help a packaging engineer or quality engineer determine an appropriate response when gels are observed.

The Challenge of Gels

Some of the most common questions related to sterile barrier systems have to do with what appears to be foreign matter associated with a package. At various times, packaging engineers or quality engineers might ask any of a number of questions: What are these particles or debris? Where do they come from? Are all of them foreign to the package? Are they on the film or in the film? At what point do I need to be concerned about them, and how concerned should I be? Do they impact the sterility of the package and the product? All of these are good questions, driven by a responsible desire to ensure patient safety and product efficacy.

The answers to these questions are not as straightforward as we might like them to be. Surface or entrapped insects, hair, and metal fragments, for instance, are clearly matters of concern and should be rejected. On the other hand, small gels (smaller than 0.5 mm²) embedded in the sealant layer of a film, while visible to the naked eye, are not generally foreign to the packaging and do not impact the performance of the package or the safety of the medical device. However, between these two extremes the answer is not always apparent.

In this white paper we will dig deeper into these matters, focusing specifically on gels. The goal is to provide a solid technical foundation that will foster data-driven decisions when addressing questions like the ones raised above.

Classification of Particulate

Before focusing more narrowly on gels, it will be helpful to discuss particulate and debris in general. Broadly speaking, particulate or debris associated with a sterile barrier system (SBS) can be categorized as foreign matter or as non-foreign matter, and they can either be (1) on one of the surfaces of a film, (2) embedded in one of the layers of a lamination or film, or (3) embedded between layers of a lamination. Figure 1 on the following page shows these three possible locations pictorially. A subset of (1) above would arise when particulate on the surface of a film is fully or partially trapped in the seal area of an SBS or preformed SBS.

Foreign matter particulate or debris has a chemical identity not related to the base materials of the lamination or film and can include hair, insects, grease or oils, metallic fragments, dust, powder, and many other things. They can appear on the surface, within a layer of a lamination, or between the layers of a lamination, and are of concern. Many (if not all) suppliers of film, laminations, and preformed SBS’s into the medical device industry have various controls in place to minimize the occurrence of foreign matter contamination. It is important that the MDM and the supplier agree upon a specification related to foreign matter and debris.

Gels, on the other hand, would generally be classified as non-foreign matter, and are always embedded within one of the layers of the lamination or film. As will become apparent later in this white paper, they can vary in size, shape, and color, and can be sporadic or appear in clusters. In the remainder of this paper, we will focus our attention on gels, and discuss their nature and origin, detection and prevention, and their impact on key SBS characteristics.

1 It will become clear later in this paper that there is one type of gel, a cross-contamination gel, that is both a gel and foreign matter.
The Nature of Gels

Most of the discussion on gels in the literature centers on polyolefin resins and films [materials like low density polyethylene (LDPE), ethylene vinyl acetate copolymers (EVAs), and linear low density polyethylene (LLDPE)]. While there is a possibility of gels in an oriented polyester (oPET) and oriented nylons (oPA) layer of a medical packaging film, it is a rare occurrence in these medical grade resins and films. Therefore, we will focus our attention on polyolefin resins and films in the remainder of this paper.²

Gels can be defined³ as “a visible dome-shaped imperfection in the film matrix due to the embedding of an incompatible material.”⁴ The size of the dome-shaped imperfection, when observed visually or felt with a finger, is always significantly larger than the underlying embedded incompatible material, and is magnified even further when the gel-containing film is laminated to another film. The incompatible materials may be of three general varieties.⁵

---

² Some of the public literature on gels erroneously includes debris like hair and paper (foreign matter). These are not gels in the proper sense of the term.
³ Polyethylene Gels: A Primer, Norman Aubee, Rolf Saetre, Tony Tikuisis, TAPPI 2006
⁴ Note that “incompatible” is not used here in the sense of “foreign,” but rather in the sense of not blending homogeneously with the matrix
⁵ Characterization of Gels in Polyethylene Film, Todd J. Obijeski and Darryl W. Dixon, TAPPI 1992
Three General Varieties of Gels

A. Unmelt/mixing Gels

These gels arise when a resin does not fully melt in the extruder barrel, or when additive master-batches aren’t thoroughly mixed and melted into the main polymer stream. These gels occur when the extrusion temperature is too low, the residence time is too short, or mixing in the extruder is insufficient to allow full melting of the polymer. These gels could also arise when the molecular weight distribution of the resin includes a high molecular weight tail. These gels should not be considered contamination, as the chemical composition of the gels is identical to the base film.

B. Cross-linked and Oxidized Gels

These come about when polymer chains break down (chain scission) and recombine (cross-link) at high temperature and/or in the presence of oxygen. These reactions are normal in all polymer extrusion operations, are controlled by the addition of additives such as anti-oxidants, and by the proper design of the extrusion process (barrel and screw design, feed block and die design, and processing conditions like extrusion rate and temperature). It is important to note that these gels can occur during the resin manufacturing process as well as during the film extrusion process. When oxygen is involved, the color of the gels can vary from amber to black (commonly called a carbon), indicating a progression in the degree of oxidation. Cross-linked and oxidized gels become more prevalent in a film when in-process scrap like edge trim is fed back into an extrusion stream. This practice is strongly discouraged in the supply chain for sterile barrier systems unless extensive work has been performed to qualify the use of in-process scrap.

C. Cross-contamination Gels

Gels of this variety would be considered foreign matter contamination, and occur when the resin stream is contaminated with a resin of a different polymer of a significantly different melt index or density. For example, polypropylene (PP) contamination of a LDPE resin would lead to gels in the LDPE film because the melting point of the PP is much higher than that of the LDPE. The PP resin pellets do not fully melt in the extruder barrel because the temperature is too low, and the residence time in the barrel is too short. However, the partially-molten PP may still be forced through the screen pack and show up in the film as gels. Cross-contamination gels can result from poor cleaning of resin handling systems in extrusion facilities (i.e., silos, conveyors, and hoppers).

---

6 Once a film has been extruded, subsequent operations such as lamination, heat sealing, and even long-term aging at 50°C will not increase the number of gels in a film. While in the case of lamination and heat sealing temperatures can approach extrusion conditions, the duration of that event is so short (on the order of milliseconds in a lamination nip or seconds between heat seal jaws) that additional gel formation is precluded.
There is clearly much more that can be said regarding the kinds of gels in polyolefin films, how their occurrence is minimized, techniques for differentiating one kind of gel from another\(^7\), and the use of detection systems on extrusion lines.\(^8\) Interested readers are directed to the references cited above for additional detail and depth.

**Process Control Issues**

It should be clear from the fore-going that while it is possible to reduce the size and frequency of unmelt/mixing gels and cross-linked or oxidized gels in an extrudate, it is not possible to totally eliminate their occurrence. The high temperatures (as high as 315°C / 600°F for extrusion lamination) and long residence times (on the order of minutes) needed during extrusion to turn resin pellets into usable film are also conducive to the creation of gels. A reputable film supplier will work closely with resin suppliers and extruder manufacturers to establish optimal operating conditions to minimize gel formation.

<table>
<thead>
<tr>
<th>Gel Size Range</th>
<th>Count Per Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ A mm(^2)</td>
<td>None allowed</td>
</tr>
<tr>
<td>&lt; A mm(^2) and ≥ B mm(^2)</td>
<td>No more than P</td>
</tr>
<tr>
<td>&lt; B mm(^2) and ≥ C mm(^2)</td>
<td>No more than Q</td>
</tr>
<tr>
<td>&lt; C mm(^2)</td>
<td>Any number allowed</td>
</tr>
</tbody>
</table>


\(^7\) Several different techniques are available to analyze the above gel types including, but not limited to, microscope-based techniques (polarized light microscopy, hot-stage microscopy, scanning electron microscopy), FTIR spectroscopy, and pyrolysis.

Gels and Sterile Barrier Systems

Now that we have carefully considered gels, and differentiated them from other debris and contamination, it is time to turn our attention to the impact of gels on sterile barrier systems. The issues to address are the potential impact on interlayer adhesion in laminations, on the sterile barrier, and on the barrier properties of the films, and what if there is a gel in a seal area? Ultimately, the question we seek to address now is, “How might gels impact product efficacy and patient safety?”

In general, the response to the above issues depends on the size of the gel. Gross gels (larger than 5 mm²) will almost certainly impact interlayer adhesion and sealability, and may also result in a hole through the polyolefin film, and therefore gels of this size are rarely permitted in resins and films in medical device and pharmaceutical packaging.

On the other side of the size range, very small gels (0.5 mm² and smaller) are generally considered to have no functional impact on the sterile barrier system because they are so small and they are embedded in film. They are visible to the naked eye, however, and will impact the aesthetic appearance of the package. In what follows we will focus our attention on intermediate gels (those larger than 0.1 – 0.5 mm² and smaller than 5 mm²).

Gels and Lamination

When a polyolefin film that contains a gel is laminated to another substrate, such as oriented polyester (oPET) or aluminum foil, the protrusion on the surface of the polyolefin film will create a high spot on that film to which the substrate needs to conform during adhesive lamination. In the case of oPET, which is dimensionally stable and won’t elastically deform during adhesive lamination, a small area around the gel may not come in intimate contact with surface of the oPET film. This creates a magnifying effect, and a gel that is actually only 1 mm² may in fact appear to be 5 mm². In the case of aluminum foil, the dome-shaped protrusion will create an indent in the ductile foil as the foil is shaped around the gel. This also creates a surface anomaly that makes the gel look larger than it really is. And if the gel is relatively large, a foil pinhole may be created. Note that this would not be a through-pinhole, since the polyolefin film would still be free of holes.

In both of these cases, the lamination will still provide a sterile barrier, and it will still provide the same oxygen and water vapor barrier as a gel-free film. Towards the higher end of the size range we are discussing (0.5 mm² < gel size < 5 mm²), the visual appearance may be acceptable if there are relatively few gels. However, if the count is more than 2 or 3 per square foot the visual appearance may no longer be acceptable. A thorough understanding of the end-use application will provide guidance on setting an appropriate limit on gel size and gel count.
Integrity Considerations

Gels in the size range we are discussing are encapsulated in the film and cannot easily be removed from the film matrix. They will not ‘fall out’ of the film and be a source of particulate, nor do they create a hole in the film. During the thermal stress of sealing the gels will remain embedded. Most film producers have conducted barrier integrity tests on film possessing high gel count. However, there is a limited amount of published data available. In terms of microbial barrier, the presence of a gel will not impact the barrier of a film so long as the gel is not so large as to have caused a hole in material adjacent to the gel. Gels in multilayer high-barrier films will have minimal impact on total package barrier (oxygen, water vapor, or CO₂).

In form-fill-seal applications, large gels have the potential to cause the pocket to blow out in the forming process. The extent to which this might occur will depend on the draw-ratio of the form, the formability of the film, the size of the gel, and the gel count. Determining an appropriate gel size specification is best accomplished through testing and discussion with the film supplier.

Conclusion

Gels are an inherent but controllable phenomenon in flexible packaging films. When they are observed in sterile barrier system films, packaging and quality engineers will be called upon to make decisions on the impact of those gels on package integrity. In this paper, we have addressed common questions and concerns, the origin and manufacturing processes that contribute to gel formation, and the potential for gels to impact the sterile barrier system so that engineers can make those decisions with data and knowledge.
SPMC Technical Group

The SPMC Technical Group involvement in establishing standards for the medical device and packaging industry is proven and longstanding. With seats at ASTM, ISO and AAMI we work, along with other packaging experts from medical device, food and consumer goods, testing laboratories, test device OEM’s, and logistics companies, to continuously create and improve consensus standards and to educate others in the value of their use.

We encourage people to contact us with questions and suggestions that can help us continue to increase awareness of standards and common issues in the packaging industry. Contact us through the FPA site at www.sterilizationpackaging.org and post a question in our FAQ area or speak with one of our member company contacts listed on the website directly.