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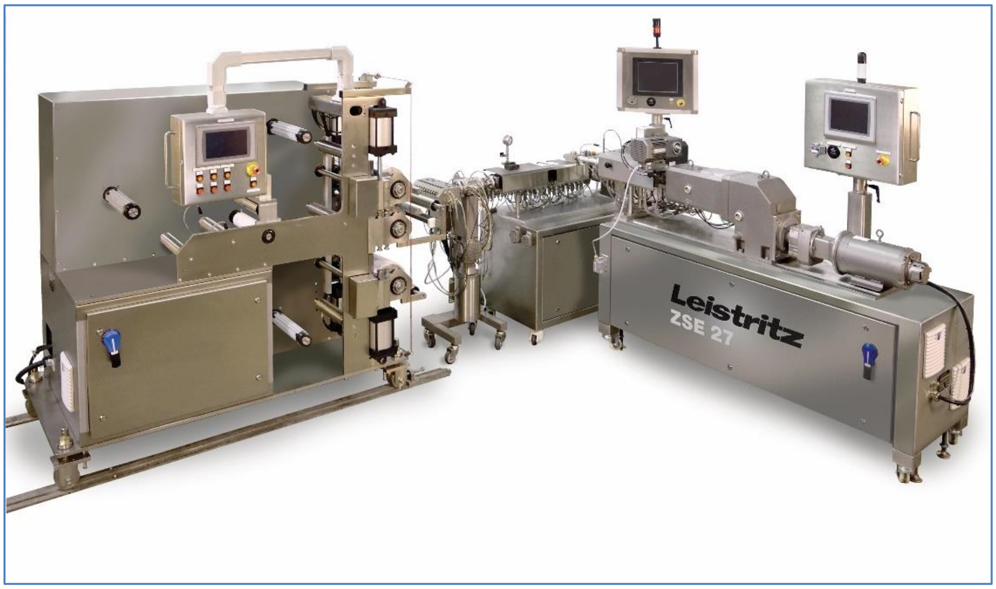
Overview of Film, Sheet, and Lamination Equipment for Life Science installations

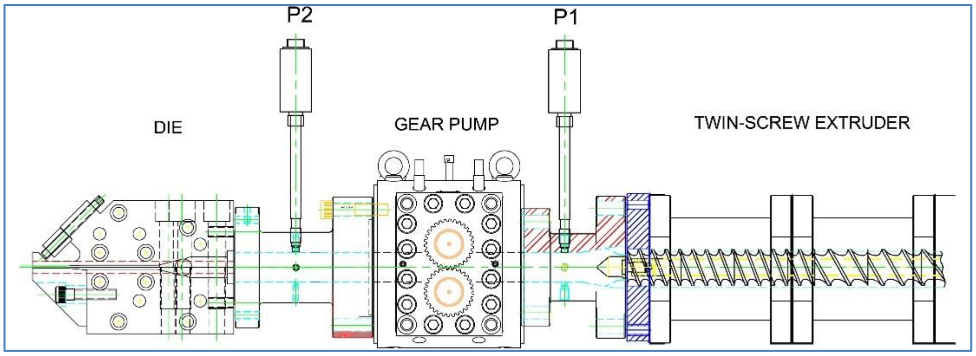
Many of the consumer products that we use every day utilize a sheet, film or laminate. Examples include roll roofing, packaging films, flexible printing plates, filtration membranes, agricultural films and tarps, frozen dinner trays (thermoformed from sheet), building insulation, kitchen countertops, battery separators, various sheets for electronics applications, interior and exterior panels for automobiles, photographic and x-ray films, etc. The same technology that is used to manufacture these types of plastics parts applies to pharmaceutical packaging and the drug delivery system itself, including transdermal and dissolvable film dosage forms.



Example of a transdermal twin screw extruder and lamination system

There are five distinct stages in any film or sheet extrusion system as follows:

1.	Material handling/metering:	Raw materials is moved from some type of container and metered into a twin screw extruder (TSE)
2.	Melting/mixing:	Formulation components and temperature are conditioned and homogenized
3.	Pressurization:	Molten polymer is pumped into the die
4.	Shaping:	Melt is deformed and oriented in the die to the final shape
5.	Finishing	Heat removal and shape control can then occur (focus of this discussion)

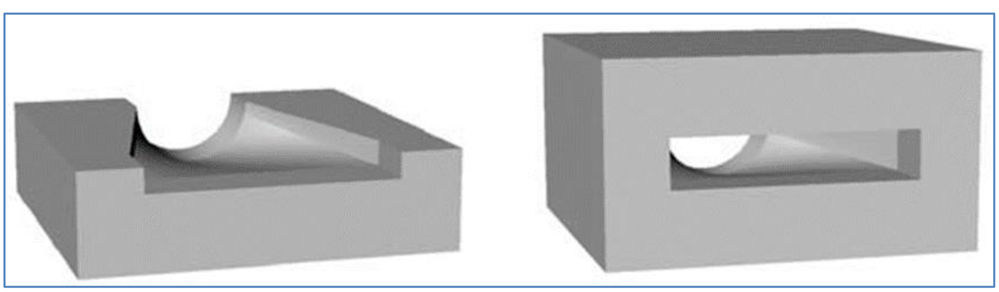


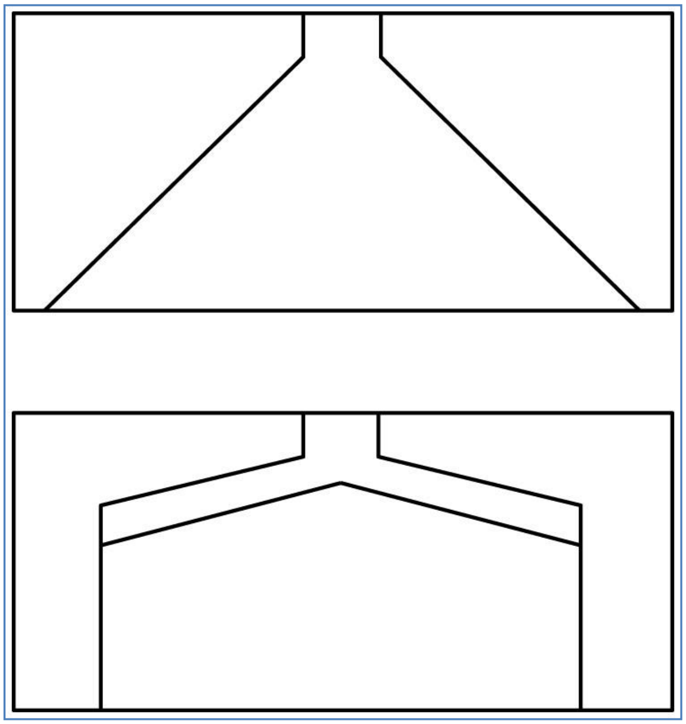
Example of the pressurization and shaping steps

As with most extrusion equipment used for Life Science pharmaceutical products, the sheet and film processing machinery is typically downsized. The initial part of the extrusion system (until the die) is considered the melt processing section. After the die is the downstream section. To optimize the web path, it is generally best to begin at the winder and work backwards. Some important equipment design parameters include:

- Extrusion throughput rate: This is typically expressed in kgs/hr
- Finished product width: This is in the transverse direction, or across the web.
- Thickness: Thinner/flexible products are called films, and thicker products are sheets
- Product tolerances: Expressed as +/- as a % or thickness dimension
- Sheet characteristics: Flexible, rigid, or semi-flexible
- Final product of the system: Will the product be wound up on a core, or cut in lengths and stored flat?
- Line speed: Determined by the rate, die width and gap, material specific gravity, etc.
- Web path: Route the material and any substrate travels from the die exit to the end of the line
- Drive system: Because the rolls directly determine the product thickness, speed control is critical. The rolls should be driven by a variable-speed motor, and have a closed-loop feedback drive for tight tolerance speed regulation
- Gear pump integration: A positive displace device at the discharge of the extruder build and stabilize pressure to the die
- Die: film or sheet (coextrusion possible)

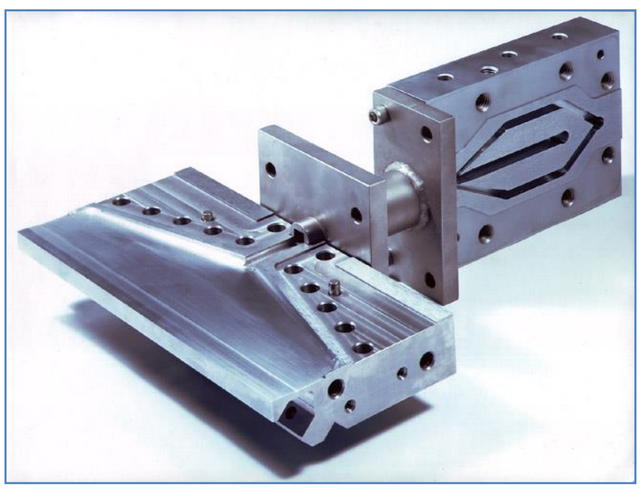
Die design: For the extrusion of flat product the material must be converted from the circular shape into a film or sheet. The balancing in this type of die needs to account for the shorter material path along the centerline versus the sides.


Transition from extruder adapter to flat film or sheet



Example of fishtail vs coat hanger internal manifold die design

Flow corrections occur in the internal manifold so that the molten material that exits the die creates a uniform melt curtain. Die lip adjustment allow for fine tuning of the final dimension, with the number and position of heat zones also being important design factors. Materials of construction include stainless steel and nickel-based alloys, and various GMP surface treatments matched to the application. Computer modeling, based on rheological characterization, can simulate the melt flow to help optimize the flow channel designs.



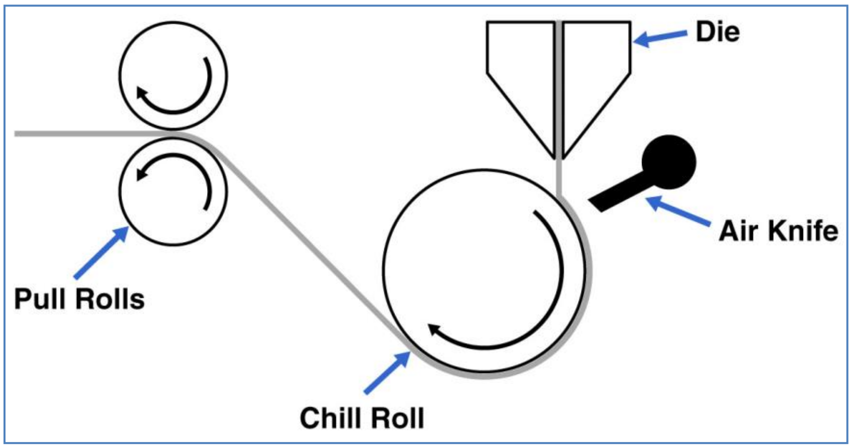
3 Layer coextrusion structure: A-B-A

In addition to mono-layer structures, coextruded film and sheet is possible when utilizing multiple extruders. For coex applications, it is best to match viscosities and melt temperatures of the different layers as closely as possible.

Equipment for thin film and laminates:

Packaging film is all around us and we see it every day. The industry standard for "film" (as compared to sheet) refers to products that are less that are less the .25 mm in thickness. A flat film die (mated to the extruder) distributes the melt into a uniform "curtain" that is discharged onto a casting roll. The temperature of the casting roll is maintained by circulating a liquid (i.e. water or oil) through a rotary union and into internal coring in the roll before it exits on the other side.

Casting roll: The casting roll is the key to the flat film process. The surface finish imparts the desired surface and can be a smooth mirror chrome for a glossy film, a medium mirror chrome, or a matte or other textured finish. Various surface treatments are available. The roll diameter is dictated by the throughput rate and the line speed. The roll is essentially a heat exchanger, and therefore cooling capacities are proportional to the roll surface area. For instance, a casting roll for 200 kgs/hr will require a much larger diameter than for 20 kgs/hr.



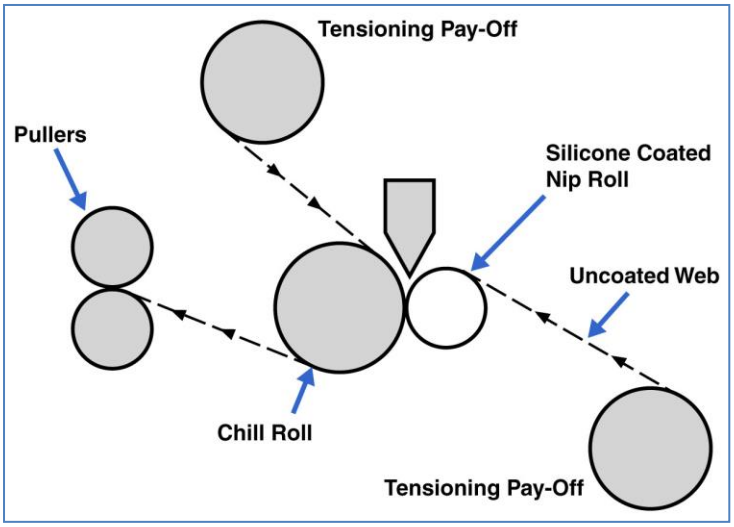
Cast film downstream schematic

After the main casting roll the film is pulled by a set of rubber-covered nip rolls. Most cast films will have an 'edge bead', meaning that the outer edges of the film will be thicker. Edge bead can be removed by a slitter station that is typically located after the nip rolls and before a winder. Slitters for films can use a simple fixed razor knife assembly or a motorized rotary blade system.

Film can be oriented in the in the machine direction by having a separate motor drive on the pull roll station to stretch the film while moving along the web path. (biaxially oriented films are also possible with alternative systems)

Roll temperature control: Rolls are maintained at a desired temperature by circulating a liquid through the internal coring of the roll. Treated water and oil are typically utilized.

Laminate stations: A film unit can be configured with laminate unwind stations to integrate substrate into the structure. The position of the unwind is mandated by the web path to introduce the substrate into the casting roll at the correct location to facilitate adhesion. The unwind shaft(s) are situated either above or below the casting roll.



Lamination schematic with 2 payoffs

Unwind designs can range in sophistication (and price) depending on the tension control accuracy required. To determine the required tension needed, the substrate properties must be evaluated carefully. A strong, thick substrate that is not prone to stretching will work with a fairly wide range of tensions. If the substrate web is thin and weak, or will wrinkle easily, then it is important to have a better control of the tension.

Air knives & edge pinners: A layer of air can get entrapped in between the film and the roll surface and cause cooling and surface quality issues. An air knife can help by discharging a 'curtain' of air directed at the film to keep it in contact with the roll. Edge pinners are similar devices, but instead of a curtain, emit a 'point' jet of compressed air at edge of the film.

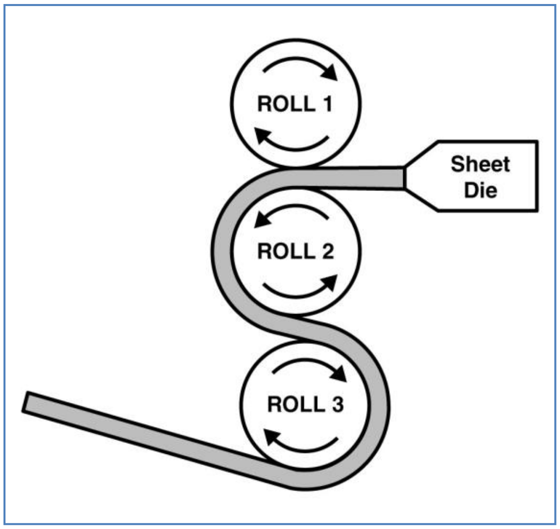
Spreader rolls: Anti-wrinkle rolls can be placed at various mounting positions to influence the film quality by stretching, spreading and allowing the web to lay flat without wrinkles. Designs include aluminum, steel and rubber bowed rolls that are supplied with and without grooves.

Winders: A variety of winders and options are available, from simple to complex. Films that require delicate tension control will require an automatic taper tension system. Other parameters include: the diameter of the roll, the weight of the final roll, whether a cantilevered design is possible, the winding speed, and the method for automatic or manual for core changeovers. Suffice it to say, winder technology warrants a much more in-depth discussion.

Simple torque winder with air chuck

Equipment for sheet production:

The industry standard for “sheet” (as compared to film) refers to products that are thicker than .25 mm. Die and roll designs are similar to cast film, with multiple rolls with rotary unions. Sheet extrusion also uses a flat die and cored cooling rolls to form the product.



3-roll Sheet stack assembly

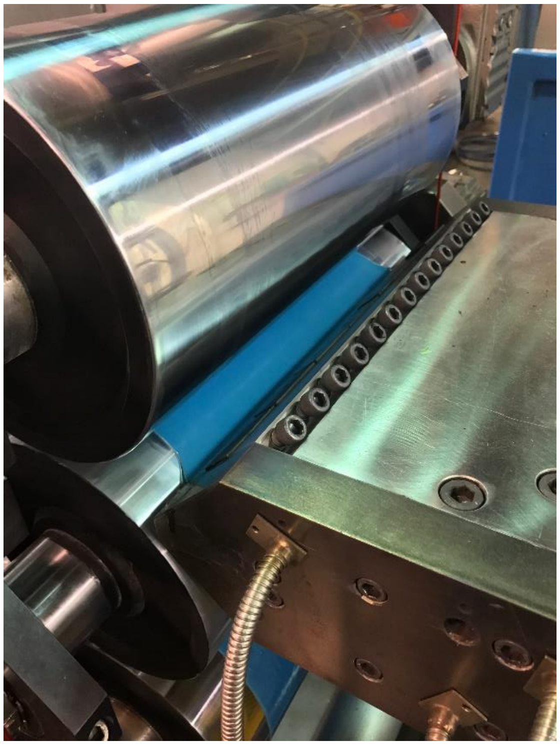
In general, sheet equipment is of a heavier construction than film machinery, as the roll nip forces are much higher. Sheet also tends to run at much slower line speeds because the product is thicker. Sheet takeoff units are made in several different configurations, including, horizontal and slanted roll stack assemblies.

Horizontal 3-roll stack assembly

A major design feature when specifying a sheet take-off is the nip pressure of the rolls, typically defined in pounds per linear inch (PLI). Low melt viscosity materials that are easily squeezable will not need much PLI force as to compared stiffer, high molecular weight formulations.

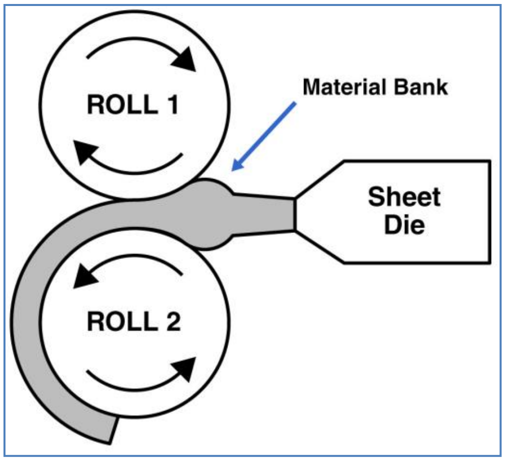
Most of the other features and auxiliary devices are similar to cast film applications, modified for thicker, heavier gauge and stiffer products.

Sheet processing tips: There are many nuances that result in a successful sheet extrusion operation. For instance, “drawdown’’, which refers to the melt curtain being pulled at a comparatively higher linear speed to draw down the dimension of the sheet, that often improves properties and results in a thinner and narrower end-product. Die dimensions need to accommodate for this drawdown effect. It is important to note that the roll gap is not necessarily set to the exact dimension as the final product gauge. This again is highly material dependent. The correct gap is generally arrived at by performing test runs with known roll gap settings, and by checking the gauge of the final sheet.



Draw down effect between die and take-off roll

Alternatively, a sheet system can operate with what is called a ‘‘rolling bank’’. This effect is created by operating the roll speeds at a slightly slower linear speed than the melt curtain. This causes a ‘‘pool’’ of molten material to continuously build up in the primary nip gap and ensures that the nip gap is 100% filled with good contact between the rolls. Because of the surface friction of the rolls, this pool tends to continuously roll over itself, hence the term rolling bank.



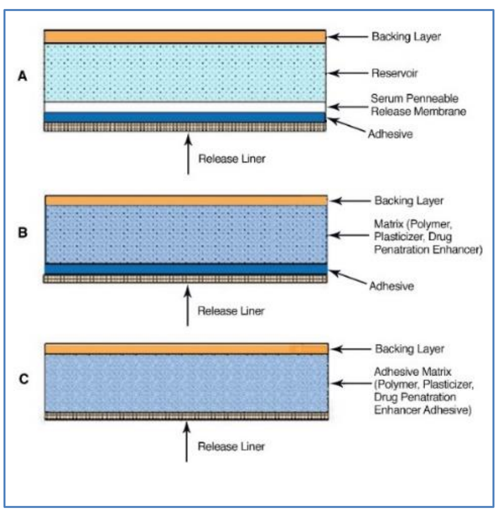
Rolling bank at primary nip

Running too large a rolling bank may cause excessive force on the rolls and induce residual stresses into the product causing surface defects. As always, the formulation and application influences what works best.

Examples of Life Science Products

Transdermal delivery systems (TDDS): Transdermal delivery is a non-invasive method of drug delivery where the medication is delivered into the body through the skin. (i.e. nicotine patches) These systems typically contain adhesive material, rate-controlling membrane, backing materials, reservoir vehicle, and release liner. In the reservoir and matrix type systems the adhesive component keeps the patch in place on the skin and has no further function. In a drug-in-adhesive system, the drug is incorporated into the adhesive.

Traditionally, matrix and drug-in-adhesive forms of TDDS have been manufactured through solvent casting. Solvent casting includes extended processing time, high costs, and environmental concerns. Comparatively, extrusion is a continuous, cost effective mixing process that does not use solvents, and increases solubility, absorption, and efficacy of poorly soluble drugs through the creation of a solid dispersion.



Example of various transdermal delivery patches

A TSE lamination system can create all parts of the TDDS using a film line. Implementing the various film manufacturing methods and techniques discussed in this chapter, it is simple to see that extrusion is a versatile option when it comes this dosage form.

Dissolvable films: Dissolvable oral thin films manufactured via melt extrusion have become popular due to their ease of use and convenience. There are several unique applications and examples including: edible oral films, soaps and face masks, and several dermal applications, including bandages, sublingual and buccal delivery systems using hydrophilic polymers with mucoadhesive properties.

GMP requirements and modifications

The technology to continuously produce a sheet or film is well proven, with literally thousands of installations in North America alone. Currently, the challenge is to downsize and apply this well-proven technology to the Life Science and pharmaceutical industries.

Various machinery builders have different degrees of experience with pharmaceutical practices. The safest approach when purchasing a GMP system is to generate a detailed User Requirement Specification for the requirements of the system and to perform equipment and testing prior to purchase.

Don’t hesitate to contact Leistritz Extrusion to prepare a quotation, schedule a test in our USA process development laboratory, or to discuss twin screw technologies in general.

We look forward to working with you in the future!

Team @ Leistritz Extrusion

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