**Pharmaceutical Bulletin 8**
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# Emulsification Properties

## Stabilizing Emulsions with Carbopol® Polymers

Carbopol®* polymers have been used in topical creams and lotions to permanently stabilize traditional emulsions for many years. Today, pharmaceutical formulations have a new series of polymers that can eliminate the struggle to find the right HLB with traditional surfactant. The polymers are called Pemulen™* polymeric emulsifiers. These novel primary emulsifiers have a small oil-loving (lipophilic) portion in addition to a large water-loving (hydrophilic) portion.

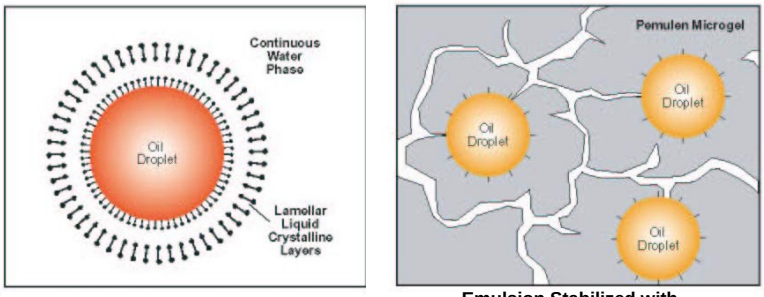
This chemical structure allows these copolymers to function as primary emulsifiers in oil-in-water pharmaceutical emulsions. Whereas Carbopol® water soluble polymers have proven useful as secondary oil-in-water (o/w) emulsion stabilizers, Pemulen™ polymeric emulsifiers can actually form o/w emulsions. The lipophilic portion adsorbs at the oil-water interface, and the hydrophilic portion swells in the water forming a gel network around oil droplets to provide exceptional emulsion stability to a broad range of oils.

## Forming Emulsions with Pemulen™ Polymeric Emulsifiers

Traditionally, ionic or nonionic surfactants stabilize oil-in-water emulsions principally by adsorbing and forming lamellar liquid crystalline layers at the emulsion interface, requiring usage levels of 3-7%. The hydrophilic-lipophilic balance (HLB) of the oil and surfactant phases must be carefully matched to insure good emulsion stability. Often polymeric hydrocolloids, such as Carbopol® polymers, are added to increase the stability of the oil-in-water emulsions by thickening and adding yield value or structure to the water phase.

Emulsions created with very low levels of Pemulen™ emulsifiers are highly stable. Oil droplets are protected and held in place as a result of the very high yield aqueous gel around each oil droplet. On forming o/w emulsions, Pemulen™ molecules form an adsorbed gel layer around each oil droplet, with the hydrophobic portions of the polymer anchored in the oil phase. Thus, when two oil droplets approach each other, a physical repulsive force is generated by the presence of these adsorbed gel layers. This mechanism is represented in Figure 1.

**Figure 1**




**Traditional Soap-Stabilized Emulsion**

**Emulsion Stabilized with Pemulen™ Polymeric Emulsifiers**

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## Benefits of Pemulen™ Polymeric Emulsifiers

Pemulen™ polymeric emulsifiers[1] are novel oil-in-water (o/w emulsifiers which provide numerous benefits to emulsions prepared with them:

**Benefits of Pemulen™ Polymeric Emulsifiers**

- Universal emulsifier of any oil into an O/W emulsion
- Excellent emulsion stability
- High efficiency / low usage levels
- Low irritancy
- Rapid release of the oil phase and medicament upon applications of occlusive emulsion layer
- Heat is not required in formulation procedures
- Effective emulsions at low oil phase loadings
- Reduction of application frequency
- Enables unusual new product forms

***Universal emulsification*** – Pemulen™ polymeric emulsifiers are water insoluble polymers that readily anchor at the oil-water interface independent of oil type. Pemulen™ polymeric emulsifiers do not depend on building liquid crystalline structures to provide emulsion stability, therefore, they can be used with virtually any oil phase, regardless of the oil phase HLB or temperature of emulsification. Oil-in-water emulsions have been made with many non-reactive, nonionic oil types, including mineral oil, volatile silicone oils, aromatic oils, fatty ethers or esters, and hydrocarbons/waxes. Oils can be emulsified at room temperature, and fats or waxes are emulsified at their molten temperature.

The following is a sample of products that have been successfully emulsified in water with 0.4% or less Pemulen™ TR-2 NF:

- Linseed Oil
- Mineral Oil
- Oleic Acid
- Perfluorinated Oils
- Coal Tar
- Silicone Oil
- Tallow
- Pine Oil
- Vegetable Oils
- Waxes

[1] CTFA name: Acrylates/C10-30 Alkyl Acrylate Cross-Polymer. Products can be generically described by the "Carbomer 1342" monograph in the USP23 / NF 18, however, Pemulen™ polymers provide additional emulsification functionality. Pemulen™ polymers are polymerized in a patented ethyl acetate-cyclohexane mixture. This solvent mixture is environmentally and toxicologically preferred to benzene and chlorinated solvents.



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***Excellent stability –*** A broad range of emulsions have remained stable in the bottle for years, even at elevated temperatures of 40°C. These emulsions are also stable to repeated freeze-thaw cycles. (See Figure 2)

**Figure 2 – Median droplet sizes of emulsion gels prepared by different methods in relation to storage time**

**At room temperature:**

| | Median Droplet Size (μm) | | | |
|---|---|---|---|---|
| | After preparation | After 1 month | After 3 months | After 6 months |
| Manual process | 300 (100 - 1000) | 250 (100 - 1000) | 300 (100 - 1000) | 300 (100 - 1000) |
| Mechanical process | 20 (10-30) | 25 (10-40) | 25 (10-40) | 25 (10-40) |

**At elevated temperature (40°C):**

| | Median Droplet Size (μm) | | | |
|---|---|---|---|---|
| | After preparation | After 1 month | After 3 months | After 6 months |
| Manual process | 300 (100 - 1000) | 300 (100 - 1000) | 300 (100 - 1000) | 300 (100 - 1000) |
| Mechanical process | 25 (10-40) | 25 (10-40) | 25 (10-40) | 25 (10-40) |

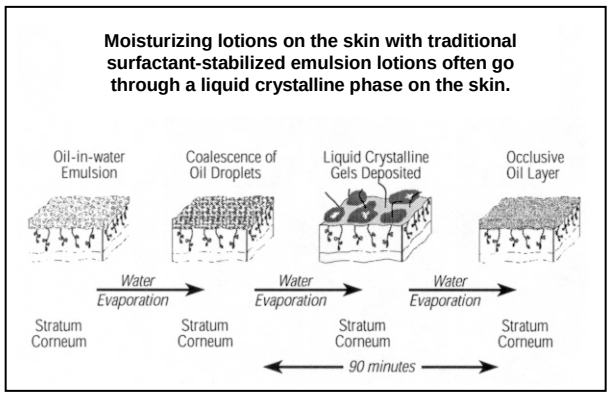
**Source: Bremecker, Klaus et al: in Die Pharmazeutische Industrie 54; 182-185; (1992)**

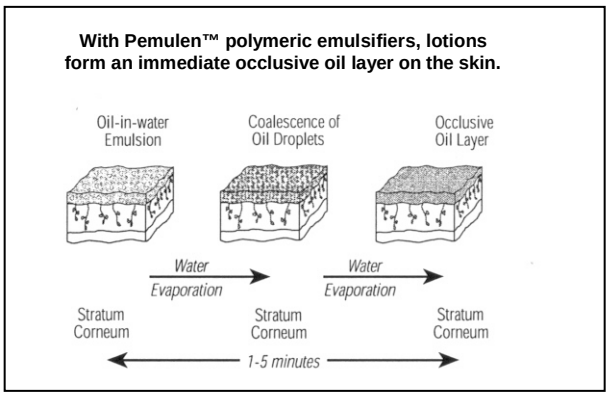
***Low irritancy / Low usage levels –*** Due to their hydrogel nature and highly efficient properties, typical usage levels of only 0.1 - 0.3% of a Pemulen™ emulsifier are required to replace 3 - 7% of traditional and potentially skin-irritating surface active emulsifiers.

***Oil phase will not re-emulsify –*** When formulated with little or no surfactant, the oil phase in a Pemulen™ emulsion can spread rapidly and cannot re-wet. Waterproof emulsions are therefore easily prepared. In traditional emulsions, upon final evaporation of the water phase, the oil layer contains high concentrations of surfactants[2], rendering the oil phase readily re-emulsifiable.

***Rapid release of the oil phase –*** Emulsions created with Pemulen™ polymeric emulsifiers have a triggered release mechanism. The acrylic hydrophilic portion of the Pemulen™ polymeric emulsifier hydrogel de-swells upon contact with the surface charge and salt content common on skin to release the oil phase and provide immediate coverage of the oil phase, eliminating the lengthy lag time seen in traditional o/w emulsions. (See Figure 3.)

**Figure 3 – Liquid Crystal Structures**




[2] Tsutsumi, H., Utsugi, T. and Hayashi, S., *Journal of the Society of Cosmetic Chemistry*, 30, 345, 1979.



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In traditional emulsions, lamellar liquid crystals, comprised of oil, water and surfactant, retard the rate of deposition of the oil phase to the substrate[3]. These liquid crystal structures persist for up to ninety minutes after application. The liquid crystal structures may be observed by polarized light microscopy. The time lag from application to the formation of the continuous oil phase is caused by the slow evaporation of the water phase from the liquid crystal structures.

***Simplified emulsion formation procedures*** – Stable emulsions can be formed by the stepwise addition of oil phase ingredients to the water phase at any temperature, including ambient room temperature, at which point all ingredients are liquid. Economies may be derived from the elimination of heating and cooling cycles during manufacture.

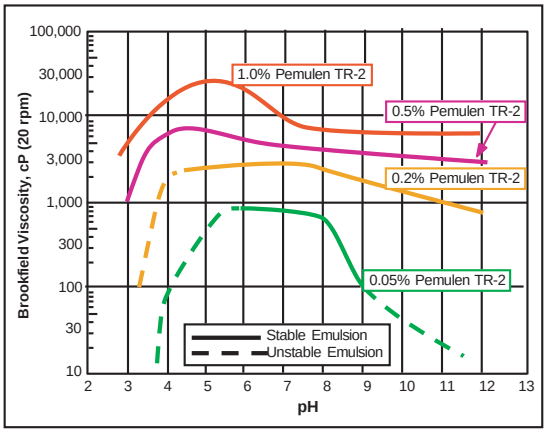
## Formulation Guidelines

***Compatibility –*** Pemulen™ polymeric emulsifiers are compatible with a broad range of nonionic or slightly ionic water soluble materials. High levels of electrolytes will prevent the normal swelling of the hydrophilic portion of the molecules, and emulsion creaming may result. (See Figures 5 - 8 on the following page). Cationic species often complex with Pemulen™ polymers, although low levels of many cationic materials are compatible and effective as spreading and wetting agents. (See TDS-124: "Cationic Skin Lotions Formulated with Pemulen™ Polymeric Emulsifiers" for more details).

***Particle size –*** Pemulen™ polymers are capable of producing extremely stable macro emulsions, even at large average oil particle sizes (approaching 1 - 2 millimeters diameter). For aesthetic reasons, it is often desirable to product small particle size (1 - 5 micron) emulsions having a high degree of whiteness, opacity and creamy appearance. Low levels (0.1 - 0.4%) of liquid medium (8 - 12) nonionic surfactants are very effective additives for achieving these oil droplet particle sizes. In addition, nonionic surfactants such as nonyl phenoxy-poly (ethyleneoxy) ethanol (Igepal® CO-530, Rhone-Poulenc) or sorbitan monooleate (Span® 80, Uniqema) are also effective. High shear mixing may also reduce particle size. In-line, on-recycling homogenizers and colloid mills should be used in *controlled moderation* to avoid degradation of the polymer's hydrophilic gel network which would contribute to gel instability.

***Emulsion formation for standard aqueous solutions – neutralization –*** Pemulen™ polymer emulsifiers are mildly acidic polymers and function best when neutralized with a suitable water soluble base to the optimum pH. The optimum pH is a function of oil loading: the lower the oil loading, the broader the acceptable pH range. (See Figure 4).

**Figure 4 – Effect of pH on Pemulen™ TR-2 NF polymer emulsion viscosity (5% mineral oil emulsions neutralized with 18% NaOH solution).**




[3] Lochhead, R.Y., Hemker, W.J. Castaneda, J.Y. and Garlen, D., *Cosmetics and Toiletries*, Vol. 101, No. 11, 125, 1986.



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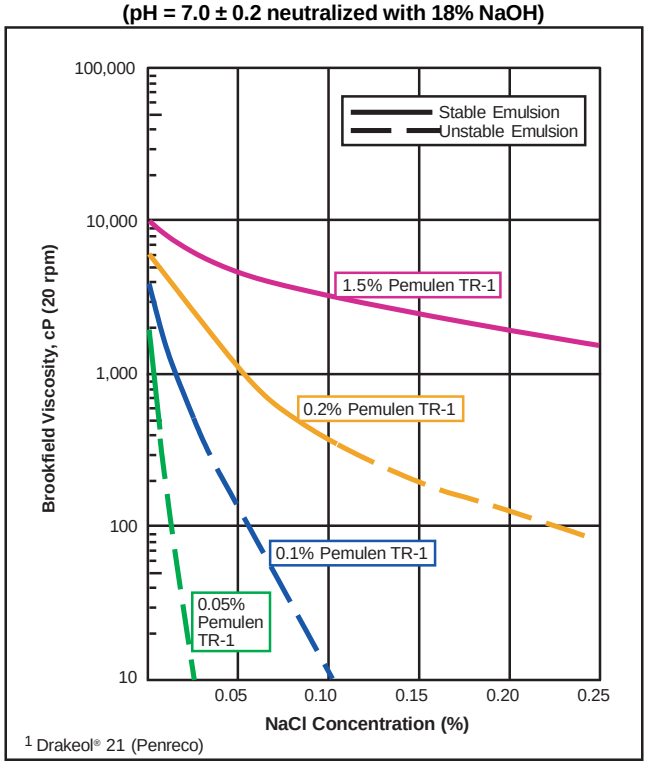
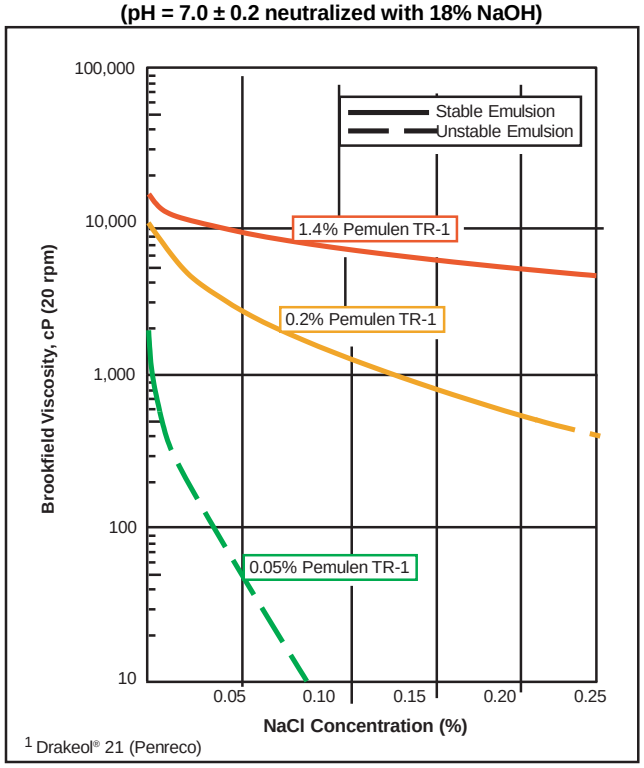
**Figure 5 – Effect of NaCl concentration on emulsion viscosity and stability for Pemulen™ TR-1 NF polymer and 5.0% mineral oil[1] O/W emulsion (pH = 7.0 ± 0.2 neutralized with 18% NaOH)**




[1] Drakeol® 21 (Penreco)

**Figure 6 – Effect of NaCl concentration on emulsion viscosity and stability for Pemulen™ TR-1 NF polymer and 30.0% mineral oil[1] O/W emulsion (pH = 7.0 ± 0.2 neutralized with 18% NaOH)**




[1] Drakeol® 21 (Penreco)

**Figure 7 – Effect of NaCl concentration on emulsion viscosity and stability for Pemulen™ TR-2 NF polymer and 5.0% mineral oil[1] O/W emulsion (pH = 7.0 ± 0.2 neutralized with 18% NaOH)**

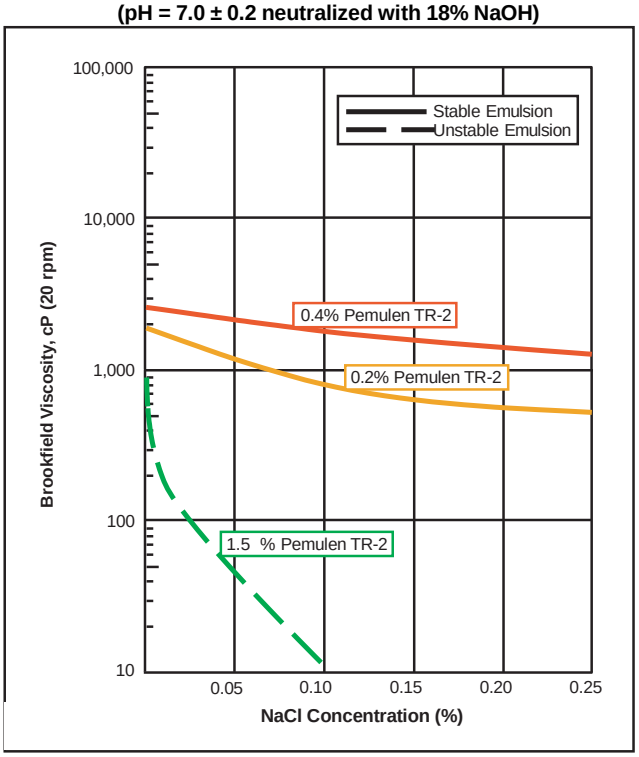
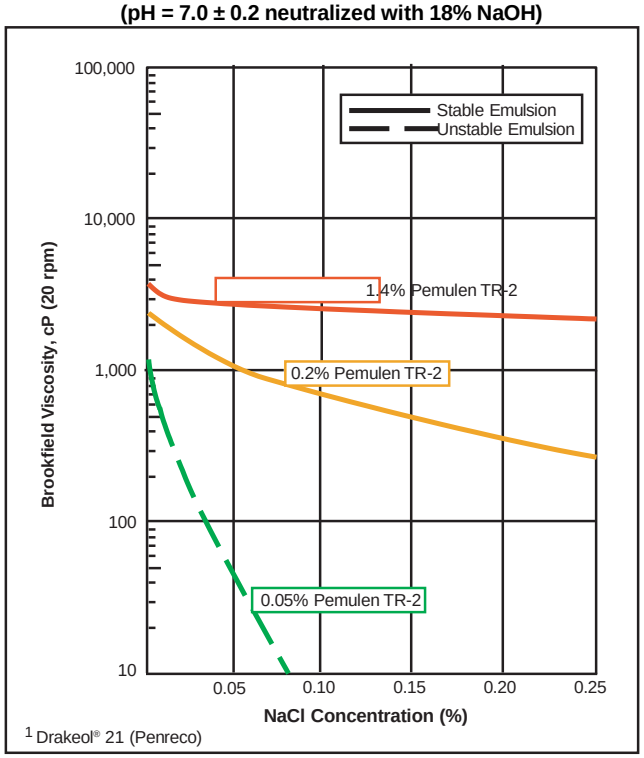



**Figure 8 – Effect of NaCl concentration on emulsion viscosity and stability for Pemulen™ TR-2 NF polymer and 30.0% mineral oil[1] O/W emulsion (pH = 7.0 ± 0.2 neutralized with 18% NaOH)**




[1] Drakeol® 21 (Penreco)



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***Moderation of breaking upon application*** **–** Emulsions prepared using Pemulen™ polymeric emulsifiers as the sole emulsifier or thickener release the oil phase very quickly upon application. This effect may not be desirable in some applications. To decrease the rate of emulsion breaking when applied, the use of a low level of a slightly surface active film former is recommended. Hydroxypropyl methylcellulose at a 0.10% concentration, or Poloxamer 181, 182 or 183 at 0.5% concentration are very effective. Formulations which contain some surfactant resulting in a relatively small particle size and higher phase volume of oil (e.g. >30%) may not require such an additive.

***Structuring / Body agents*** **–** Use of compounds that typically structure o/w emulsions at the interface, such as cetyl and stearyl alcohols and partial glycerides should be limited. Undesirable, highly cohesive textures often result, and the lyotropic liquid crystals formed by cetearyl alcohols will delay the release of the oil phase for emollient properties or protection behavior.

***Thickening*** **–** Pemulen™ polymeric emulsifiers do provide some thickening of o/w emulsion formulations. If additional body or thickening is desired, Carbopol® polymers are recommended, typically at 0.2 - 0.6% concentrations.

## Emulsification Procedure

Pemulen™ polymeric emulsifiers are adaptable to a variety of emulsion preparation methods. Pemulen™ polymer powder is most easily dispersed in room temperature oil. The oil phase is combined with the water phase containing the neutralizing alkali or amine using rapid, turbulent mixing action.

In the presence of some polar oils (aromatic or dicarboxylic acid esters) or molten oils above 60°C, Pemulen™ polymers may physically plasticize, hindering stable emulsion formation. Dispersing Pemulen™ polymers directly into the water in these cases will result in smooth, stable emulsions.

## Pemulen™ Polymeric Emulsifier Type Selection

In general, the selection of Pemulen™ polymer types are based upon the level of oil to be emulsified:

Pemulen™ TR-1 NF polymeric emulsifier is a versatile polymeric emulsifier which can easily emulsify up to 30% oil by weight, within a pH range of 4.0 - 5.5, and up to 20% oil over the pH range of 3 - 11. (See Figure 9.) While Pemulen™ TR-1 NF polymeric emulsifier thickens the water, Carbopol® polymers should be used with Pemulen™ TR-1 NF polymeric emulsifier to provide greater thickening properties where higher viscosity emulsions are required.

Pemulen™ TR-2 NF polymeric emulsifier can emulsify the highest levels of oil (up to 60 - 80% by weight) within a pH range of 4 - 8. (See Figures 9, 10 and 11.) Pemulen™ TR-2 NF polymeric emulsifier is highly effective at levels below 0.4% where the mode of emulsion application is via spray mechanism.



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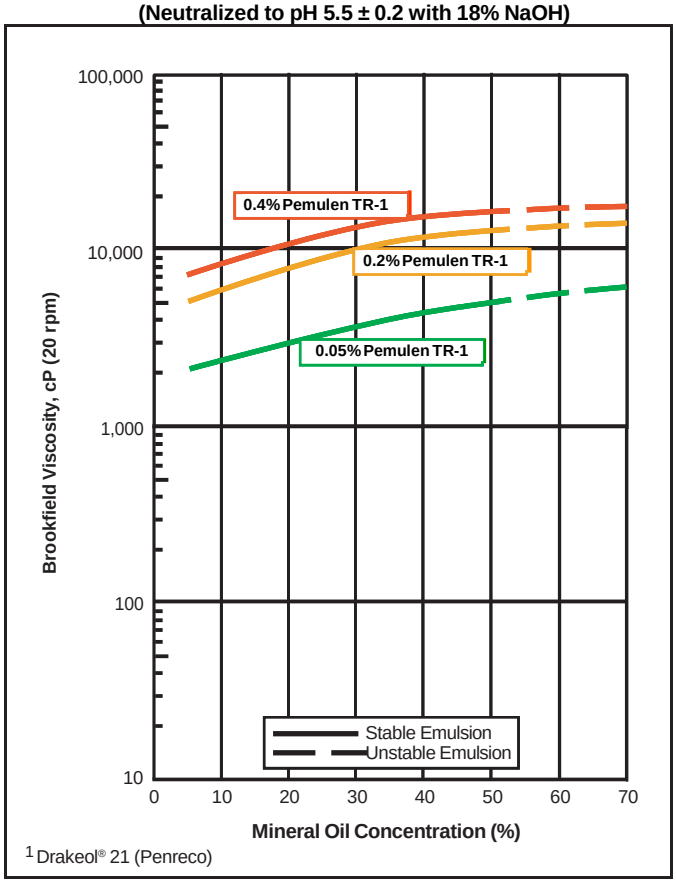
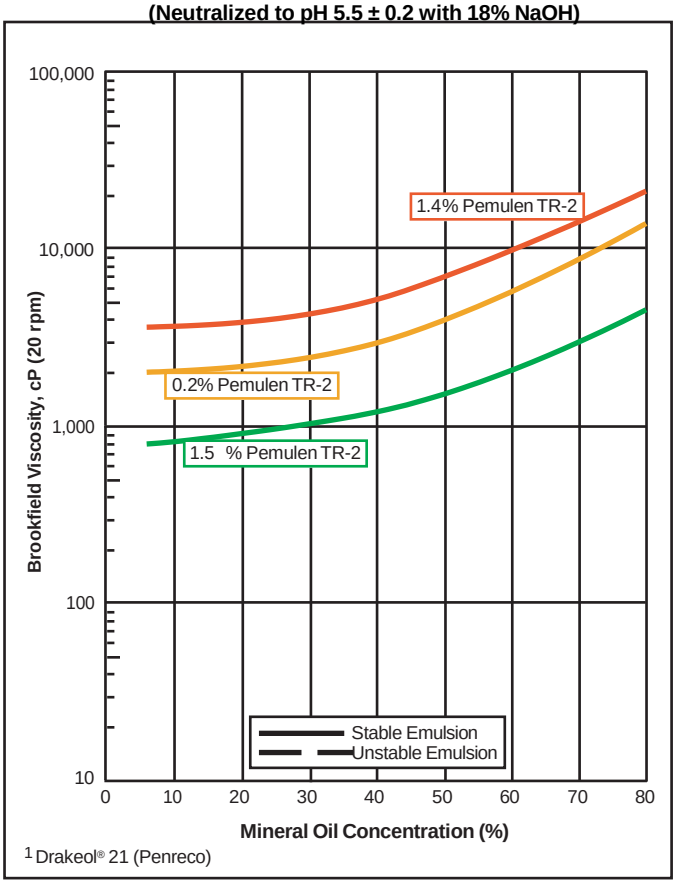
**Figure 9 – Effect of mineral oil[1] concentration on Pemulen™ TR-1 NF polymer emulsion viscosity and stability**
**(Neutralized to pH 5.5 ± 0.2 with 18% NaOH)**



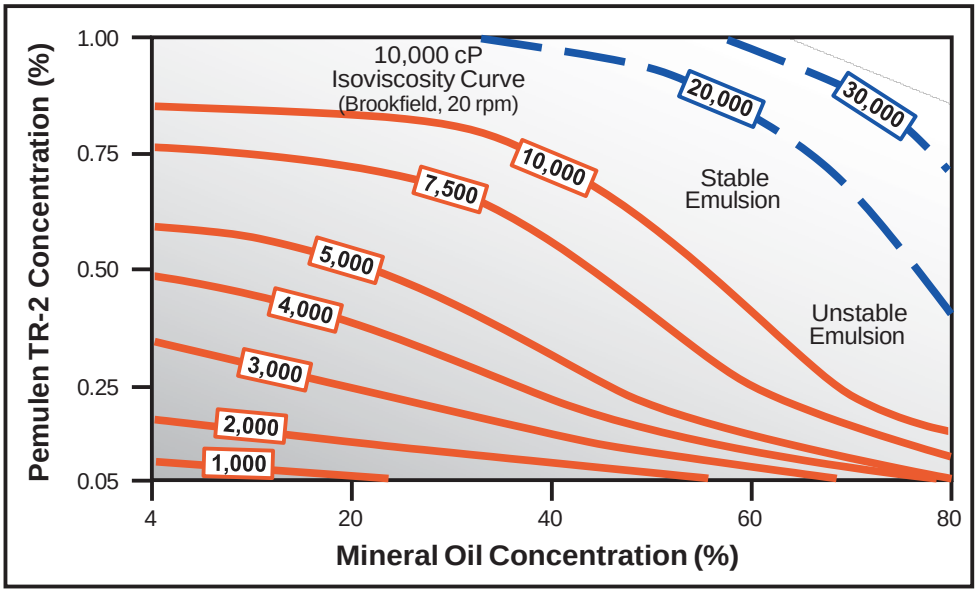

[1] Drakeol® 21 (Penreco)

**Figure 10 – Effect of mineral oil[1] concentration on Pemulen™ TR-2 NF polymer emulsion viscosity and stability**
**(Neutralized to pH 5.5 ± 0.2 with 18% NaOH)**




[1] Drakeol® 21 (Penreco)

**Figure 11 – Effect of mineral oil[1] concentration on Pemulen™ TR-2 NF polymer emulsion viscosity and stability. (pH = 5.5)**




[1] Drakeol® 21 (Penreco)



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## Testing for a Stable Emulsion

After you have made an emulsion, there are a number of different ways to test if it will remain stable over time. Here are the most common:

1. **Viscosity vs. Time –** After the emulsion is made, measure the original viscosity and periodically thereafter to detect any large changes. If a 10% deviation from the original viscosity results in less than 3 months at room temperature, this is a sign or an unstable emulsion.

2. **Centrifuge –** Subjecting the emulsion to a 5 - 10 g force for several minutes will test the resistance to creaming. Although this test exerts an artificially elevated gravitational force on the emulsions, it can determine the yield strength of the emulsion that assists in maintaining stability to phase separation.

3. **Emulsion Droplet Size Analysis –** Image (microscope) or other analytical size analysis may detect a broad droplet size distribution in Pemulen™ polymeric emulsions o/w emulsions. Unlike conventional emulsions, *this is not a predictor of emulsion instability*.

4. **Heat Storage Test –** Viscosity rise of less than 20% over original values after storage of samples at 50°C for one month indicates room temperature stability for one year. A viscosity rise is the precursor to visible creaming. Be sure there is as little head space as possible, as the water in the emulsion may evaporate and recondense, forming a liquid layer that may be mistakenly identified as a broken emulsion.



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