

# **Petrolatum and Regulatory Requirements**

**By**  
**Harold R. Faust and Edward W. Casserly**  
**Penreco<sup>®</sup>**

## **INTRODUCTION**

Petrolatum has been around since 1872.<sup>1</sup> More common names for this material are petroleum jelly or Vaseline<sup>®</sup> (a registered trademark of Unilever). It has evolved from a relatively impure waxy substance to the highly refined product that we know today.

Petrolatum is used in hundreds of different applications that range from shoe polish to dielectric lubricants to drugs and cosmetics. This paper concerns the use of highly refined petrolatum in food, drug and cosmetic applications.<sup>2</sup> We will discuss the US Food and Drug Administration's (FDA) requirements and the FDA test for polynuclear aromatic hydrocarbons (PNA's). We will also discuss the use of petrolatum in drug products and the obligations manufacturers have when selling petrolatum into the drug market. Finally, we will explain the European Union's (EU) Dangerous Substance Directive and why petrolatum is on a list of carcinogens.

## **What is Petrolatum?**

This question is not being asked from a technical point of view, but rather from a regulatory perspective. Petrolatum with CAS number 8009-03-8 has the following definition.

*A complex combination of hydrocarbons obtained as a semi-solid from dewaxing paraffinic residual oil. It consists predominantly of saturated crystalline and liquid hydrocarbons having carbon numbers predominately greater than C<sub>25</sub>.*

This is the description that you would get if you plug the number 8009-03-8 into various web sites including the EPA's Toxic Substances Control Act (TSCA) Inventory. What is important about this definition is what it does not say about petrolatum. It gives no detail about processing and more importantly it provides no criteria for purity. Therefore, this CAS number applies to unrefined, heavy, waxy materials as well as to highly refined products that meet United States Pharmacopeia (USP)<sup>3</sup> and FDA standards. There are other CAS numbers for petrolatums that do give brief processing descriptions. However, none give any type of purity criteria for petrolatum. Nor are these other CAS numbers listed on the TSCA Inventory.

## **Manufacturing and Specifications**

The components for petrolatum come from paraffinic lube oil refineries. Petrolatum can be considered as a combination of mineral oil and petroleum wax. The separation of wax components from oil involves solvent dewaxing and the filtration of the wax from a solvent-oil slurry at low temperatures. However, the best petrolatum components come from waxy oils that have not had the microcrystalline wax separated from the oil. This “natural petrolatum” has a far better propensity to hold the oil and waxy components together and therefore shows less oil bleeding or syneresis over time. This is not to say that mineral oils or waxes are not added to the petrolatum. They may be added to produce specific grades of petrolatum with slightly different physical properties.

The purification process for making petrolatum usually involves hydrogenation and/or adsorption. The hydrogenation reaction is carried out on a catalyst at high temperature and pressure. This process saturates many of the aromatic compounds and removes polar hydrocarbons such as those containing sulfur, nitrogen or oxygen. The adsorption process is accomplished by percolating the melted liquid petrolatum over an absorbent such as clay or bauxite. The product off the absorption step is lower in aromatic content, and lower in polar hydrocarbon content. As with hydrogenation, the resulting petrolatum is much lighter in color than the starting material. Most importantly, petrolatum derived from these processes passes the FDA purity test that limits the polynuclear aromatic hydrocarbon content.

## **Physical Property Specifications**

Having made a purified base petrolatum, manufacturers can then work with this base to create various grades that meet specific requirements. The USP, for example, sets a range for consistency and melting point and a maximum color in the two monographs for petrolatum, White Petrolatum USP and Petrolatum USP. The basic difference between these categories is the maximum color. White Petrolatum USP can have some yellow color but Petrolatum USP has a definite yellow color.

The European Pharmacopeia (EP) does not use the term petrolatum but it does have White Soft Paraffin that corresponds to White Petrolatum USP and Yellow Soft Paraffin that corresponds to Petrolatum USP. The physical tests in these EP monographs have slightly different methods and ranges than those in the USP monographs for petrolatum. Similar tests are also found in the Japanese Pharmacopeia and the Food Chemical Codex (FCC).

## **Purity Specifications**

The most important purity test for petrolatum is the analytical procedure for PNA's. Certain condensed polynuclear aromatic compounds have been shown to cause cancer in animals and humans. In the mid 1960's, the FDA and others undertook extensive research programs to develop a method that limited the PNA content of petrolatum and petroleum wax. The

culmination of this work led to the test that is currently found in the CFR under petroleum wax, 21 CFR 172.886(b).

Based on the recovery of model PNA's added to petroleum wax samples, Howard et al. estimated that the total PNA's "would be of the order of 0.6 ppm (excluding chrysenes and triphenylene)."<sup>4</sup> Since the absorbance maxima for petrolatum in 21 CFR 172.880 (See Table 1) are slightly higher than those for wax, the total PNA's in petrolatum are around 1 ppm if the absorbances are near the maxima.

**Table 1**  
**Petrolatum Listings in**  
**Code of Federal Regulations**

---

**21 CFR 172.880 (Direct Addition to Food)**

UV limits:

280 – 289 nm:	0.25 max
290 – 299 nm:	0.20 max
300 – 359 nm:	0.14 max
360 – 400 nm:	0.04 max

**21 CFR 178.3700 (Food Contact)**

UV limits: Same as above

**21 CFR 573.720 (Animal Feed)**

UV limits: Same as above

---

In this procedure PNA's are extracted into a mixture of dimethyl sulfoxide and phosphoric acid. After numerous washes the concentrated PNA's are measured by UV absorption in isooctane. This is the primary method for the analysis of total PNA's as described in 21 CFR 172.886(b). If the absorbances at this point in the procedure are below the limits set by 21 CFR 172.880, the sample is considered a "pass." We should point out that the 5<sup>th</sup> edition of the FCC, effective January 1, 2004, references this same purity requirement for Petrolatum.<sup>5</sup> If the sample fails at this point, 21 CFR 172.886(b) permits (in the secondary part of the method) additional "clean up" to remove interfering compounds. Since this optional part of the procedure involves numerous manipulations, reliable results may be difficult to obtain. It is industry practice to run the primary part of the procedure only. If the sample does not pass, additional processing is called for rather than additional testing. Using only the primary part of the procedure provides a margin of safety in limiting the total PNA's in the product. It also avoids exposure to benzene, which is used in the secondary part of the test but not in the primary part. Benzene is known to cause leukemia in humans so its use in routine lab procedures is avoided where possible.

## Pharmaceutical Applications

We will now turn our attention to the uses of petrolatum in drug products. This is limited primarily to topical applications to the skin or certain mucous membranes. First we need to distinguish between cosmetic and drug applications. The main difference is that drug products have an active ingredient and certain claims of effectiveness can be made based on that active ingredient. Cosmetics can alter the appearance but they should not have any physiological effect on the skin.

When petrolatum is used in drug products it can be either an active ingredient or an excipient. An excipient is the non-active ingredient in the formulation. It may also be referred to as the “carrier” or “vehicle” for the active ingredient since it may comprise 95% or more of the total formulation. But petrolatum can also be considered as the active ingredient in Over The Counter (OTC) drugs. Petrolatum, along with other ingredients, was listed by the FDA in a 1983 publication in the Federal Register called the Tentative Final Monograph for Skin Protectants.<sup>6</sup> This made it possible for any formulation containing 30% to 100% petrolatum to make the label claim of a skin protectant. Such products are OTC drugs and therefore are regulated by the FDA as drugs. In June of 2003 the FDA published the “Final Rule” in the Federal Register<sup>7</sup> that listed petrolatum as a skin protectant as long as the concentration was in the range of 30% to 100%. The CFR will be updated in June 2004.

Examples of drug products where petrolatum is the active ingredient can be found in any drugstore. Jars of petroleum jelly will normally show on their labels: Active Ingredient: White Petrolatum USP. The same language can be found, for example, on diaper rash preparations and in ointments intended for use on hemorrhoids.

## FDA Requirements for Drug Manufacturers

Drug products, both prescription and OTC, are closely regulated by the FDA. They are certainly regulated at the site where the final drug is formulated and packaged. But they are also regulated at the site where the bulk drug is manufactured. This means that petrolatum manufacturers that claim that their products are USP have certain obligations. Their manufacturing sites must follow current Good Manufacturing Practices (cGMP) as outlined in 21 CFR 211. A partial list of the requirements is shown in the table below. The manufacturing site must also be registered with the FDA using Form 2656 and the Form needs to be sent to the FDA every year even if there are no changes to report. The products that are used as drugs must also be included in an FDA form (Form 2657) that allows the FDA to track their status.

**Table 2**  
**Partial List of cGMP Requirements**

Personnel Training	Instrument Calibrations
Batch Records	Label Control
Reserve Samples	Documentation of Procedures
Stability Testing	Audits

Since the manufacturing site is registered with the FDA, it becomes subject to unannounced inspections by the agency. Customers that use petrolatum in drug products will also audit petrolatum manufacturers. These audits are conducted to verify that the petrolatum is manufactured under cGMP. Not only are these customer audits more frequent than the FDA audits they often comprise a team of inspectors who may spend up to two days at a facility. In effect, drug customer audits are surrogates for an FDA inspection, since the customer must maintain their own certifications.

While a plant that complies with current ISO standards would have a good start on meeting cGMP requirements, ISO standards are only the foundation. ISO standards require facilities to have written procedures and requires them to be followed. With cGMP, facilities must show that procedures are in place that would prevent problems from occurring. The concept of cGMP is to be sure that drugs are safe and effective for humans and animals. It is not enough that the bulk drug meets the standards in the USP and the FDA. The processing, testing, packaging, etc. are just as important as the specifications.

Section 501 (a) (2) (B) of the Federal Food, Drug and Cosmetic Act provides that a drug is deemed to be adulterated if the product is not produced following cGMP. There are frequent reports in the media of non-compliance by large and small drug companies that cost those companies millions of dollars in fines and recalls.

### **Recent Regulatory Activity**

Over the past decade mineral oils and petroleum waxes have come under greater scrutiny from regulators, particularly those in Europe. Petrolatum is implicated because it can be considered a combination of mineral oil and wax. The concern was raised because it was shown that very small portions of the hydrocarbons were absorbed by a particular strain of rat, Fisher 344, during feeding studies. The hydrocarbons accumulated in the liver and mesenteric lymph nodes of the Fisher rats and resulted in the normal immune response that any foreign body would cause. Absorption was found in other animals but not to the extent found in the Fisher rat. All of the animals were able to clear the oil from their systems over time when it was eliminated from their diets.

After reviewing these data regulators at the FDA have not changed the food status of petrolatum or of petroleum wax and mineral oil. European regulators have limited the food contact of mineral oils and waxes and therefore petrolatum.<sup>8</sup> Microcrystalline wax and high viscosity mineral oils, the two major components of petrolatum, were rated as having the least effect on the animals by JECFA<sup>9</sup> (Joint Expert Committee of the World Health Organization and the Food and Agriculture Organization of the United Nations) and by the European Union's (EU) Scientific Committee on Food.<sup>10</sup> These views are reflected in new regulations with higher Allowable Daily Intakes (ADI's) for high molecular weight mineral oils and microcrystalline wax. It is important to point out that after years of animal feeding studies there is no evidence that these materials have been implicated as carcinogens. A review of this work was presented at the 2002 NPRA meeting in Houston.<sup>11</sup>

## EU and the Dangerous Substance Directive

The final topic for discussion originated in the European Union in 1976. Directive 76/769/EEC<sup>12</sup> provided a mechanism for tracking commercial chemicals used within the EC. Its purpose is similar to TSCA, which is administered in the US under the EPA. This Directive restricts the marketing and use of certain dangerous substances and preparations.

The Dangerous Substance Directive has various lists of chemicals but the one of most concern to us is the so-called CMR list. This is a consolidated list of substances that are considered carcinogens, mutagens, or toxic to reproduction. A subpart of the list, Category 2 Carcinogens, includes seven entries for petrolatum. One of them is for oxidized petrolatum, five others describe various processing schemes for making petrolatum, and one of them is the description and CAS number that is commonly used in commerce. None of the descriptions specifically defines purity in terms of limits to the PNA content. We presume that the petrolatum entries were put on this list because unrefined petrolatum products could contain the PNA compounds that are known to be carcinogenic.

Fortunately, the originators of the CMR list recognized that there are refined grades of petrolatum that are essentially free of PNA's. They provided for this with the note "N" next to each petrolatum entry. Note N states:

*The classification as a carcinogen need not apply if the full refining history is known and it can be shown that the substance from which it is produced is not a carcinogen.*

We have interpreted this to mean that refined petrolatums that pass the UV limits in FDA regulation 21 CFR 172.880 are exempt from the consequences of being on the CMR list. The importance of the FDA test that we discussed earlier is now clear. Not only do these petrolatums meet the UV limits for direct food contact but we have made the test more severe by not using the secondary part of the procedure. Petrolatum manufacturers would rather refine a product further than to resort to the second part of 21 CFR 172.886 (b) to get a pass.

In addition to the note N there is a note L that is also part of the CMR list. Although Note L does not appear with the petrolatum entries it is part of the CMR list. Note L states:

*The classification as a carcinogen need not apply if it can be shown that the substance contains less than 3% DMSO extract as measured by IP 346.*

Any petrolatum that passes 21 CFR 172.880 will pass IP 346<sup>13</sup> by several orders of magnitude. But IP 346 is not intended for refined petrolatum. It is used primarily for lube oils and waxy products such as unrefined petrolatum. We have run this test and found that even our feedstocks (prior to processing) pass quite easily. This is probably a reflection on the extensive use of hydrogenation in lube oil refineries today.

It is clear that refined grades of petrolatum are exempt from the CMR list. Not only do they pass the most stringent tests for PNA content but there are no positive human or animal data that

show that they are carcinogenic.<sup>14</sup> This was established by the International Agency for Research on Cancer (IARC)<sup>15</sup> and more recently for mineral oil and microcrystalline wax, components of petrolatum, in acute and chronic animal feeding studies.<sup>11</sup>

## **EU and the Cosmetic Directive**

The Dangerous Substance Directive previously did not present a major problem for petrolatum because technically it did not apply to materials used in the cosmetic and pharmaceutical industries. These areas are exempt because they are regulated by other agencies in the EU. A similar exemption technically applies in the US under TSCA.

But the EU agency that regulates cosmetics recognized that the Dangerous Substance Directive is intended to limit the public's exposure to carcinogens and some cosmetic materials are on the list. In February of 2003, the 7<sup>th</sup> amendment to the cosmetic directive<sup>16</sup> included a ban on the use of materials listed in the CMR that might be found in cosmetic products. Again, the FDA's test for PNA's provides a firm basis for the exemption of refined grades of petrolatum from the CMR list and therefore such petrolatums can be used in cosmetics in the EU.

Although we have shown why petrolatum is safe for use in food, drugs, and cosmetics the fact remains that it is still found on the CMR list. This is difficult to explain for a product that has the same name in the USP and in the Code of Federal Regulations. Petrolatum is also listed in the International Cosmetic Ingredient Dictionary (INCI)<sup>17</sup> as the appropriate term for the labeling of cosmetic ingredients. Both in the EU and in the US, cosmetic products must show the ingredients on the labels. This presents a dilemma for cosmetic companies that market in the EU. Even though the cosmetic companies understand why refined petrolatum is not carcinogenic it would be difficult to explain to consumers who may learn that the petrolatum in their hand cream is also listed as a carcinogen.

## **Future Challenge**

The challenge for the petrolatum users and producers is what to do about the name "petrolatum". There are alternative names such as "Soft Paraffin", "Petroleum Jelly", "Refined Petrolatum" or "Purified Petrolatum". But it is not a simple matter of just changing the name. The term petrolatum is well entrenched in the food, drug and cosmetic industries. The CFR uses petrolatum in titles to the three regulations shown in Table 1 and in numerous other entries where petrolatum is permitted for specific uses. The USP has the two petrolatum monographs and because of that petrolatum is documented in numerous drug applications with the FDA. Since petrolatum is the official name in the INCI Dictionary, petrolatum is not only found in cosmetic company documents but it is also listed on countless cosmetic labels.

This paper has demonstrated that refined petrolatum meeting established specifications is safe for use in food, drug and cosmetic products. It is our challenge to make sure that this message is loud and clear and to deal with any changes in nomenclature that may be necessary.

## References

1. Chesebrough, Robert A., "Improvement in Products from Petroleum," US Patent 127,568 June 4, 1872.
2. For a recent review of petrolatum in cosmetics and drug applications, see Morrison, David S., "Petrolatum: A Useful Classic," *Cosmetics & Toiletries* 111(1):59, 1996.
3. The United States Pharmacopeia 26 – National Formulary 21, United States Pharmacopeial Convention, Inc., Rockville, MD, 2002 "Petrolatum," p. 1441 and "White Petrolatum," p. 1442.
4. Howard, John W.; Haenni, Edward O.; and Joe, Frank L., Jr., "An Ultraviolet Absorption Criterion for Total Polynuclear Aromatic Hydrocarbon Content of Petroleum Waxes in Food Additive Use," *Journal of the AOAC* 48(2):304-315, 1965.
5. Food Chemical Codex, 5<sup>th</sup> edition, January 1, 2004, 327.
6. Federal Register, 48. No.32, February 15, 1983, 6832.
7. Federal Register, 68. No. 107, June 4, 2003. 33362
8. Council Directive 89/109/EEC of 21 December 1988 OJ L 40 11.2.1989, p. 38 relating to plastic material and articles intended to come into contact with foodstuffs. Last amended by Commission Directive 2002/72/EC of 6 August 2002 OJ L220 8.15.2002, p. 18, and corrected by OJ L 39, 13.2.2003, p. 1.
9. "Toxicological Evaluation of Certain Food Additives and Contaminants: Mineral Oils (Food-Grade), Paraffin Waxes and Microcrystalline Waxes", Food Additives Series 35, Prepared by The Forty-Fourth Meeting of the Joint FAO/WHO Expert Committee of Food Additives (JECFA), 1996. Geneva: World Health Organization.
10. SCF (1995) "Opinion on mineral and synthetic hydrocarbons" (expressed on 22 September 1995). CS/ADD/MsAd/132-Final. Brussels, European Commission.
11. Twerdoc, Lorraine, "Food Grade White Oils and Waxes - Update on Recent Research and Regulatory Review," NPRA 2002 Lubricants and Waxes Meeting, LW-02-130,
12. Council Directive 76/769/EEC of 27 July 1976 OJ L 262, 27.9.1976, p. 201 relating to restrictions on the marketing and use of certain dangerous substances and preparations. Last amended by Commission Directive 2003/53/EC of 18 June 2003 OJ L 178, 17.7.2003, p. 24. See Also: Council Directive 67/548/EEC of 27 June 1967 OJ 196, 16.8.1967, p. 1 relating to the classification, packaging and labeling of dangerous substances. Last amended by Commission Directive 2001/59/EC of 6 August 2001 OJ L 225, 21.8.2001, p.1.



13. IP Standards for Petroleum and its Products, Institute of Petroleum, London, "Polycyclic Aromatics in Petroleum Fractions by Dimethyl Sulfoxide – Refractive Index Method", IP 346.
14. Oser, B. L.; Oser, M.; Carson, S. and Sternberg, S. S., "Toxicologic Studies of Petrolatum in Mice and Rats," *Toxicology and Applied Pharmacology* 7:382-401, 1965
15. International Agency for Research on Cancer. IARC Monographs on "Mineral Oils," Vol. 33, p. 87, 1984 and Supplement 7, p. 252, 1987. Lyon, France.
16. Council Directive 76/768/EEC OJ L 262, 27.7.1976, p. 169 on the approximation of the laws of the Member States relating to cosmetic products. Last amended by Council Directive 2003/15/EC of 27 February 2003 OJ L66, 11.3.2003, p. 26.
17. International Cosmetic Ingredient Dictionary and Handbook, published by The Cosmetic, Toiletry, and Fragrance Association (CTFA), Ninth Edition, 2002.