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Mineral oils are petroleum derived substances, produced through vacuum distillation at temperatures between ~300°C – ~600°C. In order to be placed on the market these products must be non-carcinogenic. All refinement processes designed to eliminate carcinogenicity of mineral oils are based on the principle of elimination of the substance groups associated with carcinogenic activity, i.e. PACs, which include PAH (polycyclic aromatic hydrocarbons) and aromatics that may contain N or S in the ring structure. Traditionally the resulting product is tested for carcinogenicity using a bioassay. The golden standard has been the mouse skin painting assay. This assay is the most relevant to study the process of carcinogenesis and its relevance to human health because available data show that dermal studies are significantly more sensitive than those via the oral route. Mouse skin painting studies have also been important in understanding the toxicity of two types of mineral oil aromatic hydrocarbons (MOAH). The first type includes the 3-7 ring PACs associated with potential carcinogenic effects that are found in the 340-535°C boiling range (at vacuum distillation). The second type, includes highly alkylated aromatic compounds (single or multi-ring systems, but predominantly 1-2 rings) which are not biologically active and thus non-carcinogenic. This shows that there are oils and related products which can have MOAH but are not carcinogenic due to their properties dictated by manufacturing; for example, there is a direct relationship between molecular weight (a function of boiling point) and MOAH content.

The current industry standard to assess carcinogenicity of mineral oil is the IP346 method. It is a non-animal method capable to distinguish the two types of MOAH, and is validated against a large data base of mouse skin painting studies. This is the only existing analytical method that has biological significance and predictive value when assessing potential carcinogenicity of MOAH in mineral oils. Therefore, the IP346 is a clear reflection of refinement efficacy by providing an in-situ direct link between manufacturing conditions and biological activity of the tested sample. If the IP346 is < 3%, the material and its subsequent derivatives are not considered carcinogenic and they can be released for further processing to fulfil technical specifications and other regulatory requirements for sensitive applications in the pharma, cosmetics and food industry.

In conclusion, the basics of mineral oil refinement, the toxicological data base and the historical developments that led to the establishment of IP346 and other regulatory tests must be properly understood. Based on this, PAC can be MOAH but not all MOAH is necessarily PAC. Thus, because MOAH is contextual, instead of focusing on what can be measured, we strongly advocate to rather measure what

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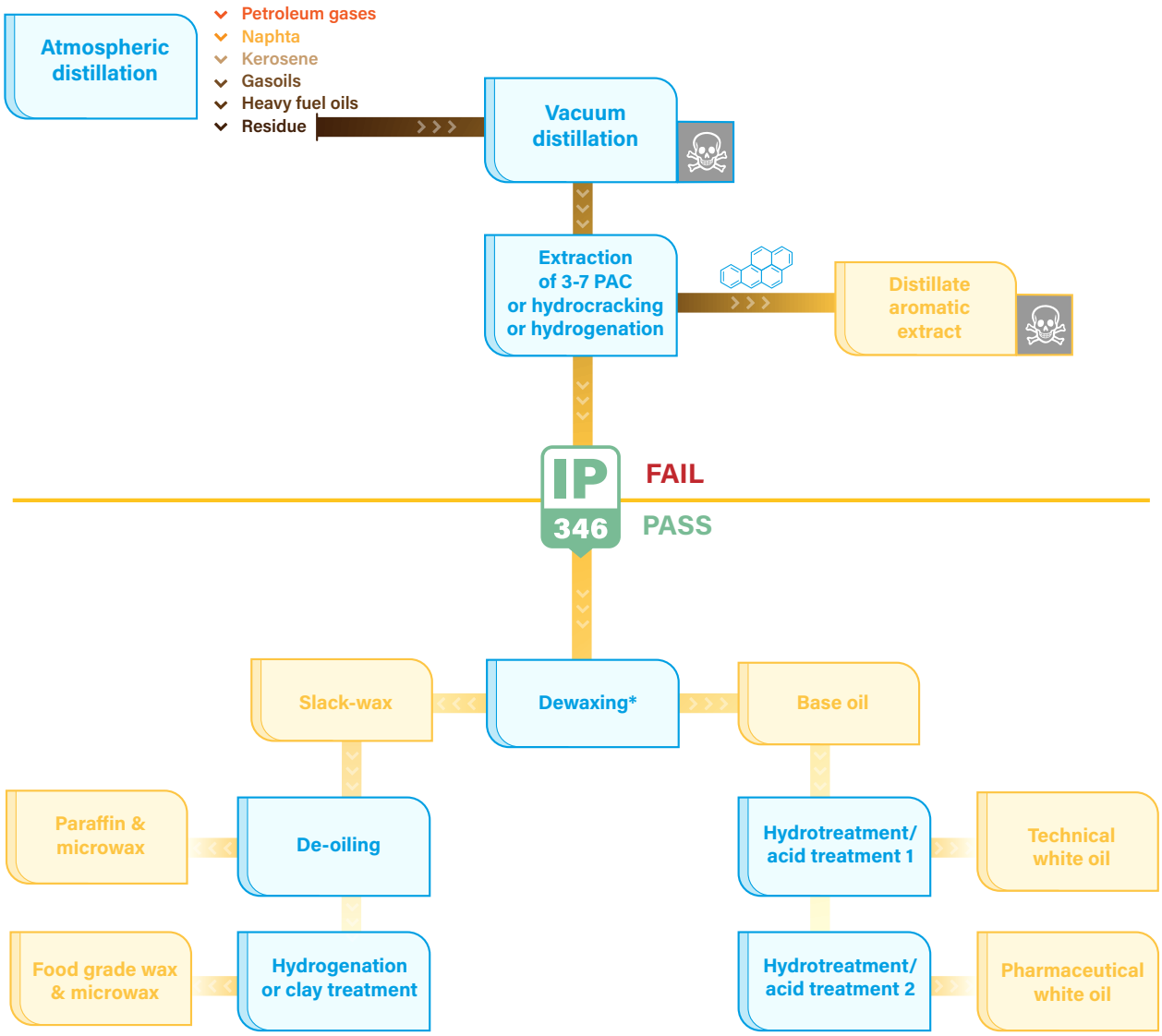
needs to be focused on, i.e. 3-7 ring PACs.

Applying the above-mentioned production and quality assurance processes ensures the safety of mineral oil compounds intentionally used in consumer goods like food, cosmetics and pharmaceutical products.


Atmospheric distillation
Petroleum gases
Naphta
Kerosene
Gasoils
Heavy fuel oils
Residue
Vacuum distillation
Extraction of 3-7 PAC or hydrocracking or hydrogenation
Distillate aromatic extract
IP 346
FAIL
PASS
Slack-wax
Dewaxing*
Base oil
Paraffin & microwax
De-oiling
Hydrotreatment/ acid treatment 1
Technical white oil
Food grade wax & microwax
Hydrogenation or clay treatment
Hydrotreatment/ acid treatment 2
Pharmaceutical white oil

Refining operation	Refining process	Product	Safety qualifier (PAC % content)
Carbon# range selection	Atmospheric and vacuum distillation	 Distillate or vacuum gas oil	Carcinogenic: IP 346 ≥ 3%
Polycyclic Aromatic Compound (PAC) removal	Solvent extraction and/or catalytic hydrotreatment		
Waxy hydrocarbons separation	Solvent dewaxing or catalytic dewaxing	  Base oil and slack-wax	Non-carcinogenic: IP 346 < 3%
Purification	Hydrogenation or acid/clay treatment	  **Technical white oil,** white oil, paraffin wax and micro-crystalline wax	Pharmacopeia tests
Petroleum jelly manufacturing	Blending and optional purification	  White petroleum jelly and yellow petroleum jelly	