Excipients & Raw Materials for Pharmaceutical Industry

pcc

More than Chemistry

Table of content

01 / RAW MATERIALS FOR API SYNTHESIS

RAW MATERIALS FOR API SYNTHESIS

Chlorine derivatives

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
Monochlorobenzene PF	Non-applicable	108-90-7	Semi-product for API production	Liquid	Non-applicable
Orthodichlorobenzene PF	Non-applicable	95-50-1	Semi-product for API production	Liquid	Non-applicable
Monochloroacetic acid 80% Ultra-Pure	Non-applicable	79-11-8	Semi-product for API production	Liquid	Non-applicable
Monochloroacetic acid 100% High-Pure, flakes	Non-applicable	79-11-8	Semi-product for API production	Flakes	Non-applicable

Monochlorobezene and Orthodichlorobenzene

Monochlorobezene (MCB) also known as chlorobenzene is a colourless, volatile, water-insoluble liquid with a light, pleasant almond fragrance. It belongs to the family of organic halogen compounds, formed by the direct chlorination reaction of benzene. In the pharmaceuticals industry it is used, among others, in:

- paracetamol synthesis (paraaminoacetylphenol)
- production of vitamin B6
- production of zoledronic acid (a drug in the treatment of osteoporosis in postmenopausal women and in men who have an increased risk of bone fractures)
- chlorfenoksamine (a drug used as an antiallergic and anti-aging agent, an analogue of diphenhydramine)
- among others it is also known as high-boiling-point solvent in industrial scale synthesis

Orthodichlorobenzene (ODCB) also referred to 1,2-Dichlorobenzene belonging to the same group of chlorine derived products formed by addiction of two chlorine atoms to benzene. ODCB is a colourless liquid that is poorly soluble in water but can mix with most organic solvents. In the pharmaceutical industry mostly well known a high – boiling – point solvent.

Monochloroacetic acid

Monochloroacetic acid 80% Ultra-Pure (80% MCAA U-P) is a product of the highest purity available, in which the DCAA content does not exceed 90 ppm. It is intended for use primarily in higher value added applications such as personal care and via Esterification in pharmaceutical applications where the DCAA content is critical to the quality of the final product. Monochloroacetic acid 80% U-P is highly reactive and is used as a raw material for many important organic compounds.

Company offers also Monochloroacetic acid 80% H-P (80% MCAA H-P) which is a high purity product characterised by DCAA <500 ppm. This grade is avaliable in a liquid form of 80% water solution 80%MCAA H-P, and solid form of flakes 100% MCAA H-P.

Monochloroacetic acid is an important intermediate for building blocks in the chemical industry and is widely used in a large number of organic synthesis processes. This is due to its high reactivity. Both chlorine in the α position and carboxyl group exhibit reactivity in a number of organic reactions, easily forming esters and amides and undergoing many possible substitutions of the chlorine atom. It has a pungent odour, is easily soluble in water, ethanol, methanol, acetone, benzene, chloroform, dimethylsulfoxide, and dimethylformamide. It is poorly soluble in hydrocarbons and their halogenated derivatives.
In the pharmaceutical industry, mainly used as MCAA Ethylester or Methylester for the production of:

- ibuprofen,
- diclofenac sodium,
- piracetam,
- caffeine,
- vitamins (e.g., vitamin B6),
- glycine,
- malonates.

Monochloroacetic acid chloride, which is a monochloroacetic acid derivative, is a precursor of adrenaline (epinephrine).
Monochloroacetic acid is produced in a continuous way. The first stage is the chlorination of acetic acid. The second stage of the process is hydrogenation in which most of the dichloroacetic acid (DCAA) is removed. In the third step of the production process unreacted acetic acid and other liquid contaminations are evaporated. This production step leads to a higher concentrated product of High Pure quality with DCAA not higher than 500 ppm. These products are diluted with distilled water into 80% water solution (80% MCAA H-P) or solidified in the flake form (100% MCAA H-P Flake). The highest quality is reaching during the crystallization process. Crystallization decrease DCAA contamination from 500 ppm to 90 ppm. Therefore Ultra - Pure quality of MCAA is received by dissolving High Pure flakes into 80% water solution known as Monochloroacetic Acid 80% Ultra - Pure.

Phosphorous derivatives

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
Phosphorus Trichloride PF	Non-applicable	7719-12-2	Semi-product for API production	Liquid	Non-applicable
Phosphorus Oxychloride PF	Non-applicable	10025-87-3	Semi-product for API production	Liquid	Non-applicable

Phosphorus trichloride

Phosphorus trichloride is a colourless, fuming liquid with a sharp characteristic odour that may resemble hydrogen chloride. PCl3 is a high-quality intermediate/raw material. Thanks to the high reactivity of phosphorus-chlorine bonds, it has become an excellent substrate for phosphoric and chlorinated chemicals, widely-used in the chemical and pharmaceutical industries. Its reactivity allows the use of PCl3 for the synthesis of, inter alia, active substances (API – Active Pharmaceutical Ingredient).

Main use of Phosphorus trichlorine

A phosphorus introducing agent to the substrate molecule through the formation of phosphites as well as their subsequent reaction – to form e.g., phosphonates (including hydroxyphosphonates and aminophosphonates), which are inhibitors of many enzymes, acting as transition-state mimetics;

Chlorination reagent, used in substitution reactions of hydroxyl groups with a chlorine atom; activator in coupling reactions, converting carboxylic or sulphonic / sulphinic acids into their chlorides (more reactive derivatives), conjugated to various nucleophiles (e.g., alcohols to form esters or amines to form amides);

A substrate for the synthesis of catalysts, where it acts as a building block for ligands.

The above-described processes are used, inter alia, for the synthesis of drugs based on sulphonamide derivatives (phosphorus trichloride converts sulphonic acids into amides, e.g., chlorthalidone – a diuretic, sulfadiazine – bacteriostatic).

Phosphorus trichloride is also a key substrate in the synthesis of bisphosphonates using the method of von Bayer and Hoffmann. Bisphosphonates are used as bone diseases therapeutic agents (e.g., osteoporosis), inhibiting bone resorption and increasing its mass, e.g., alendronate, risedronate, and etidronate).

Phosphorus oxychloride

Phosphorus oxychloride is a colourless liquid with a sharp, very characteristic odour. $POCl_3$ is a high purity intermediate/raw material which, thanks to its high reactivity, is an excellent substrate for the synthesis of phosphorus and chlorine compounds, widely-used in the chemical and pharmaceutical industries. Its reactivity allows the use of $POCl_3$ for the synthesis of, inter alia, active substances (API – Active Pharmaceutical Ingredient).

Main use of Phosphorus oxychloride

Phosphorus introducing agent to the substrate molecule through the formation of phosphates (phosphorylation);
Chlorination reagent, used in substitution reactions of hydroxyl groups with a chlorine atom;
Activator in coupling reactions, converting carboxylic or sulphonic / sulphinic acids into their chlorides (more reactive derivatives), conjugated to various nucleophiles (e.g., alcohols to form esters or amines to form amides);
A substrate for the synthesis of catalysts, where it acts as a building block for ligands;
Reagent in cyclisation processes, e.g., in the process of isoquinoline synthesis using the Bischler-Napieralski procedure.

The above-described processes are used, inter alia, for the synthesis of drugs based on isoquinoline derivatives (phosphorus oxychloride allows the occurrence of intramolecular aromatic electrophilic substitution, e.g., spasmolytic drugs – drotaverine). The phosphorylation process, for example, leads to the synthesis of B vitamins, and nucleotides are formed in the reaction with nucleosides (e.g., fludarabine phosphate aimed at the treatment of leukemia).

Important notice:
Dangerous goods – transport and storage in original packaging protected from moisture.
Products are double use items according to the UE Directive 428/2009 dated 5 May 2009.

02 / EXCIPIENTS FOR PHARMACEUTICAL FORMULATIONS

EXCIPIENTS FOR PHARMACEUTICAL FORMULATIONS

Macrogols – Polyethylene Glycols

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	MOLECULAR MASS [g/mol]	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
POLIkol 300PF	Macrogol 300	25322-68-3	Polyethylene glycol	300	Liquid	conforms
POLIkol 400PF	Macrogol 400	25322-68-3	Polyethylene glycol	400	Liquid	conforms
POLIkol 600PF	Macrogol 600	25322-68-3	Polyethylene glycol	600	Liquid	conforms
POLIkol 1500PF	Macrogol 1500	25322-68-3	Polyethylene glycol	1500	Solid in form of wax or flakes	conforms
POLIkol 3350PF	Macrogol 3350	25322-68-3	Polyethylene glycol	3350	Solid in form of wax or flakes	conforms
POLIkol 6000PF	Macrogol 6000	25322-68-3	Polyethylene glycol	6000	Solid in form of wax or flakes	conforms

PEG's

PEG's (polyethyleneglycols) belong to the group of non-ionic, tasteless substances, which are characterised by a non-toxic profile. PEG's are supplied in a wide variety of molecular weight grades.

PEG's with a low molecular weight up to 1000 are colourless or almost colourless liquids at room temperature. Polyethylene glycols with a molecular weight higher than 1000 g/mol are solid white waxes also available in flakes form. The melting point of solid PEG's form is in the range between 50 - 60°C.

Main advantages for using Macrogols in final dosage forms are:

Solubilisation

PEG's are perfect solvents for multiple substances which are insoluble in water, for instance: anilina, benzene, chloroform, pyridine, and methanol, therefore PEG's are widely-used as solvents and solubilisers for many active ingredients in pharmaceutical liquid or semi-liquid formulations.

Improvement in bioavailability for active ingredients

Polyethylene glycols are making complexes with multiple active substances which significantly improves their bioavailability. On the other hand, for some substances PEG's may contribute to the deactivation process. Taking that into account the usage of PEG's as a solvent has to be proven by research every single time.

Rheology modifiers

These substances have become a powerful tool for adjusting the viscosity level of the final formulation.

Good thickeners

Makes them an efficient additive for eye and/or ear drops.

Lubricating and binding properties

They are used in solid formulations like tablets or capsules, and tablet coatings

Formulation of stable ointments basis

Blending pasty or solid PEG's with liquid PEG's will lead to a white pasty ointment with good solubility in water and good dissolving properties which are suitable for plenty of API (Active Pharmaceutical Ingredient).

High stability

Easy mould release, good storage conditions are improved by using solid PEG's with high molecular mass for the production of suppositories and globules, additionally good solubilising properties improves solubilisation property.

ROKAnols TPF – Macrogols Cetostearyl Ethers

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
ROKAnol® T6PF	Macrogol 6 Cethostearyl Ether	68439-49-6	Polyoxyethylene (6) Cetostearyl Ether	Solid in a form of wax	conforms
ROKAnol® T12PF	Macrogol 12 Cethostearyl Ether	68439-49-6	Polyoxyethylene (12) Cetostearyl Ether	Solid in a form of wax	conforms
ROKAnol® T20PF	Macrogol 20 Cethostearyl Ether	68439-49-6	Polyoxyethylene (20) Cetostearyl Ether	Solid in form of wax or flakes	conforms
ROKAnol® T25PF	Macrogol 25 Cethostearyl Ether	68439-49-6	Polyoxyethylene (25) Cetostearyl Ether	Solid in form of wax or flakes	conforms

ROKAnols OPF – Macrogol Oleyl Ethers

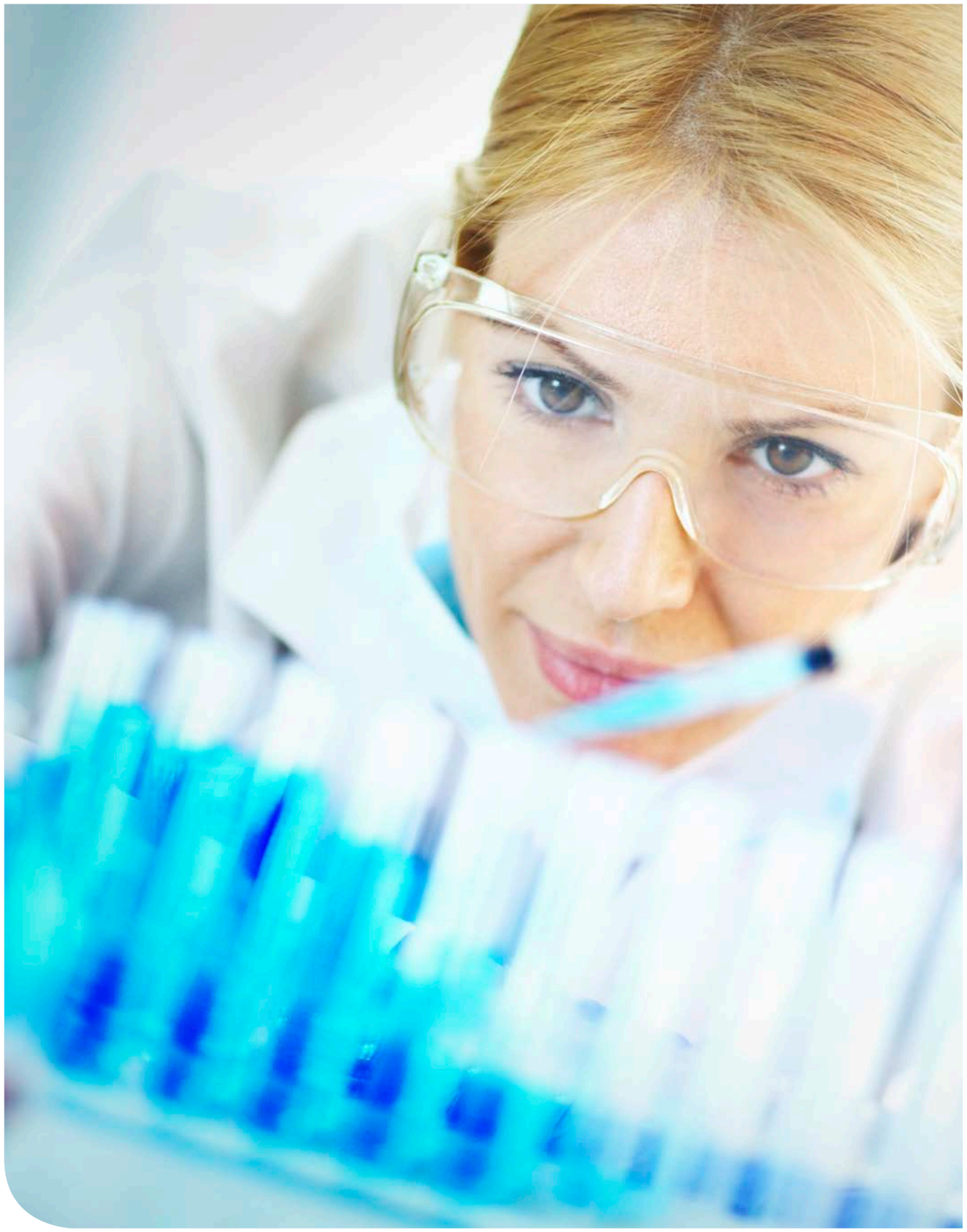
PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
ROKAnol® O10PF	Macrogol 10 Oleyl Ether	9004-98-2	Polyoxyethylene (10) Oleyl Ether	Solid in a form of wax	conforms
ROKAnol® O20PF	Macrogol 20 Oleyl Ether	9004-98-2	Polyoxyethylene (20) Oleyl Ether	Solid in a form of wax	conforms

These group of products are ethoxylated derivatives of oleyl and cethostearyl alcohols with a strong hydrophilic character, making it an ideal additive for preparing stable oil-in-water (O / W) emulsions. Possessing very good emulsifying properties, it can be used in the process of preparing emulsions at room temperature. This is important while using high temperature sensitive ingredients.

ROKAnols TPF and **ROKAnols OPF** show significant dispersing and stabilising properties which are important for adding API in a solid forms.

Common applications for ROKAnol OPF & ROKAnol TPF

- Antiseptic ointments
- Ointments
- Creams
- Oils
- Spray dressings



ROKAcet R36PF – Macrogol Glycerol Ricinoleate

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
ROKAcet R36PF	Macrogol Glycerol Ricinoleate	61791-12-6	Catstor Oil Ethoxylated	Clear, yellow viscous liquid or semi-solid	conforms

ROKAcet R36PF belongs to the group of nonionic surfactants and is characterised by good solubilising and emulsifying properties for pharmaceutical formulation. The product is in line with the current European Pharmacopeia Monograph for Macrogol Glycerol Ricinoleate which corresponds to the USP monograph for Polyoxyl 35 Castor Oil.

- ROKAcet R36PF is recomended to use as a solubiliser for preparing stable emulsion for oral, topical, parental application
- Very good emulsifier for active substances like: Miconazole, Hexetidine, Clotrimazole
- Emulsifier widely used in formulations containing ingredients like vitamins: A, D, E, K

This type of substance in a highly purified version is also used as a solubility enhancer for injection and infusion preparations.

ROKacet HR40PF – Macrogolglycerol Hydroxystearate

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
ROKAcet HR40PF	Macrogolglycerol Hydroxystearate	61788-85-0	Castor Oil, Hydrogenated, Ethoxylated	White to yellowish paste	conforms

ROKAcet HR40PF is produced during ethoxylation of Hydrogentated Castor Oil. It is characterised by very good solubilising properties used for the production of aqueous solutions of vitamins A, D, E, K. The product improves production of clear and stable aqueous formations once added to other hydrophobic substances like some API's or essential oils. It improves the stability of formulation and bioavailability for API's. It is widely-used for oral and topical application because of its odourless and tasteless characteristics.

ROKAfenol N9PF – Nonoxynol-9

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
ROKAfenol N9PF	Nonoxynol-9	127087-87-0	Nonylphenol, Ethoxylated	Clear or opalescent oily liquid	conforms

ROKAfenol N9 belongs to the group of non-ionic surfactants, this product varies in a number of repeating ethoxy (oxy-1,2-ethanediyl) groups. Rokafenol N9 is widely-used as an active ingredient in most spermicidal creams, jellies, foams, gels, and films. It is sold in most over-the-counter spermicidal products. Many models of condoms are lubricated with Nonoxynol-9 solutions. In this role, it has been promoted as a backup method for avoiding pregnancy and a microbicide for sexually-transmitted diseases in the event of condom failure. Nonoxynol-9 appears in almost all brands of diaphragm jellies and contraceptive sponges as the active ingredient.

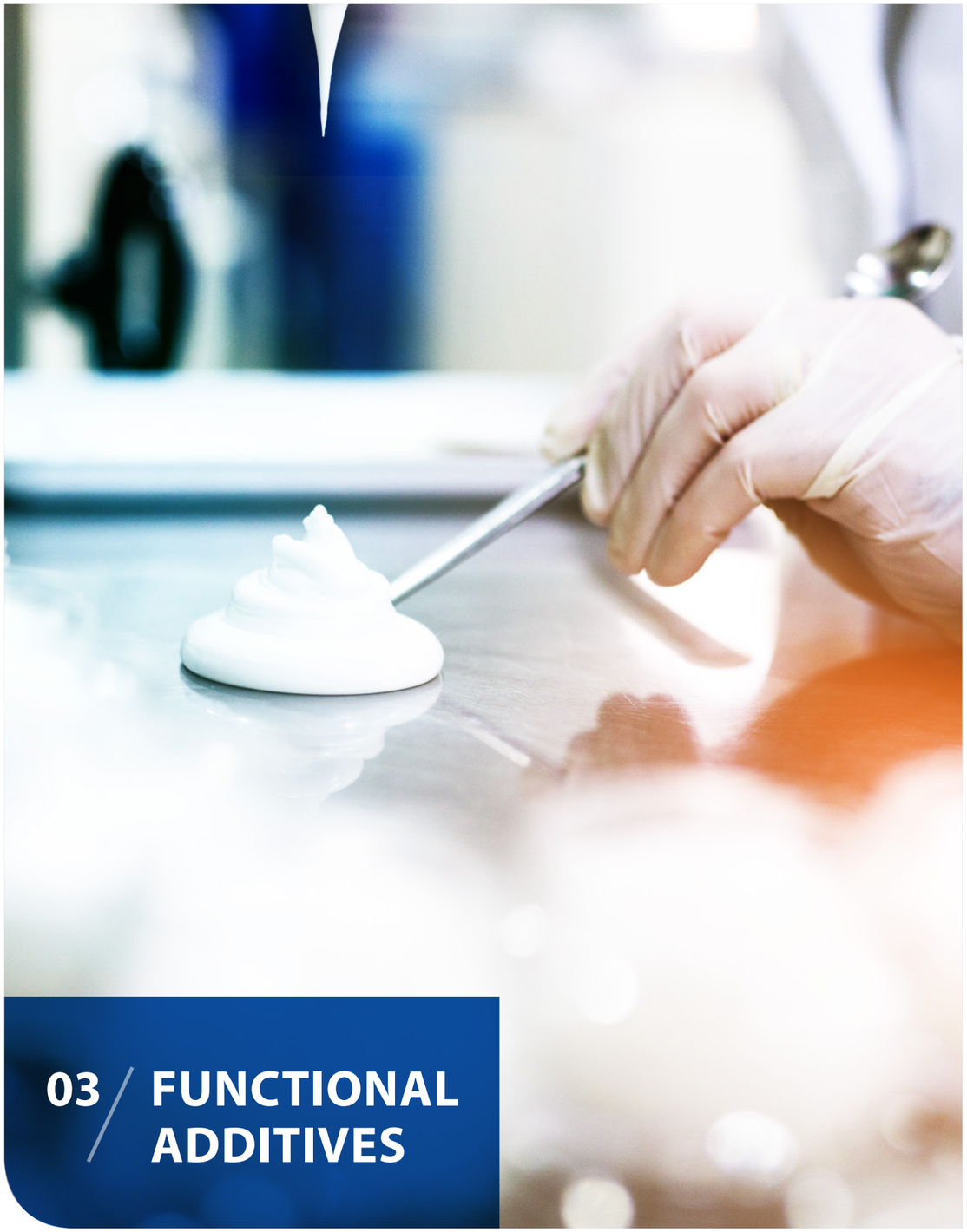
It is sometimes used as an ingredient in shaving creams because it helps to break down skin oils that normally protect hair from moisture. It also appears in medicinal products for topical use aimed at relieving muscle and joint pain associated with arthritis, bruises, sprains and strains.

ROKwinol 20PF – Sorbitan Monolaureate Ethoxylated

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
ROKwiniol 20PF	Polysorbate 20	9005-64-5	Sorbitan Monolaureate, Ethoxylated	Clear liquid	conforms

ROKwinol 20PF is an ethoxylated sorbitan ester containing approximately 20 moles of EO. These product is in line with the current monograph of European Pharmacopeia for Polysorbate 20. The product is a nonionic emulsifier and O/W type co-emulsifier, applied to emulsification of oils, waxes and solvents of cosmetic and pharmaceutical formulations. These is an excipient added to final drug dosage forms in order to provide suitable consistency. Mainly used as a binder, diluent or base for pills, tablets, creams. These product also finds application in the pharmaceutical and cosmetic industry in lotions, medical preparations (vitamin oils, vaccines, intravenous preparations).

Polysorbate 20 is frequently used as an excipient in medicinal products aimed at clinical areas such as ophthalmology or nephrology.



03 / FUNCTIONAL ADDITIVES

FUNCTIONAL ADDITIVES

Caustic soda – Sodium Hydroxide Flakes PF

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
Sodium hydroxide flakes PF	Sodium hydroxide	1310-73-2	Intermediates in pharma production, pH control	Solid (Flakes)	conforms

Sodium hydroxide in solid form, also called caustic soda, is an inorganic chemical compound belonging to the strongest alkali. In solid form, it is a white substance with crystalline appearance (flakes). It has hygroscopic properties.
This product is characterized by high quality and purity, which confirms compliance with the current edition of European Pharmacopoeia.

Caustic soda is mainly applicable:

- in the production of salicylic acid and sulfonamides
- in the production of sodium ascorbate
- in the production of iodoform used as a raw material (sodium carrier) API synthesis (including in the production of polopyrine, salicylic acid, sulfanilamides)
- as an excipient in the production of medicinal product for topical use in the form of ointments and creams. Aqueous solution of sodium hy-droxide is used to neutralize the carboxylic groups, and thus to the cross-linking of gelling agents, e.g. polyacrylic acids in therapeutic gels. This increases the availability of active ingredients in hydrogel preparations.

Hydrochloric acid min. 37% PF

PRODUCT NAME	MONOGRAPH NAME	CAS	CHEMICAL DESCRIPTION	APPEARANCE	COMPLIANCE WITH Eur.Ph MONOGRAPH
Hydrochloric acid min 37% grade PF	Hydrochloric acid concentrated	7647-01-0	synthesis catalyst, pH controller semi product for API's	Liquid	conforms

Hydrochloric acid min. 37% PF (HCl) is a chemical compound that is an aqueous solution of hydrogen chloride gas. It has strong corrosive properties, a strong, irritating odour, and colourless to pale yellow. Hydrochloric acid pure grade is produced by direct synthesis by burning chlorine in hydrogen and then absorbing hydrogen chloride into water.
Offered ultra pure grade of hydrochloric acid with pharmaceutical quality in line with Eur.Ph monograph.
Pharmaceutical industry uses hydrochloric acid as:

- a catalyst for synthesis
- pH control
- deionisation of water and as a reducing agent (for example in the production of ascorbic acid and para-aminobenzoic acid)

PCC Group
We build value through sustainable innovation

Each project or venture with a long-term success story shares one common thing – it's based on in-depth market research and on the knowledge acquired through years of experience. It is knowledge and experience that enables us to constantly aim higher and deliver greater value through dynamic and sustainable world-wide development of the PCC Group.

The companies, operating as a part of the PCC Group, act with responsibility and care. We only embark on new business challenges when we are certain that we have the skills and knowledge to achieve success. We operate in three major markets: chemicals, energy and logistics. Several dozen business units, managed by PCC SE, work in synergy to generate the greatest possible competitive advantage in both local and international markets. Each day nearly three thousand professionals contribute their energy, and effort, to secure the sustainable development of the PCC Group. The key element of our strategy is to ensure the development of each individual business unit through taking advantage of innovative technology and new market applications. We achieve our goals in a sustainable and responsible way – we care about the environment and the society within which we operate.

We are always ready to reach our strategic goals. Efficient and dynamic management helps our employees to fully develop their potential and therefore enhances the overall PCC Group value. Joint enterprises and individual initiatives of our companies are the results of the entrepreneurship culture promoted within the PCC Group. Our philosophy is built on simple values - integrity, trust and reliability. We believe that following those principles is the only way to build a long-term competitive advantage.

The PCC Group currently employs nearly 3200 people. We operate in 17 countries, in 39 different locations around the world. Our portfolio includes eight basic segments. Individual operational responsibility is assigned to seven of them - Polyols, Surfactants, Chlorine, Specialty Chemicals, Consumer Products, Energy and Logistics. Each of these segments is supported by 19 business units, all under the management of the PCC Group.

The divisions, segments and business units of the PCC Group

Divisions	Segments	Business units
Chemicals	Polyols	• Polyols • Polyurethane Systems
Chemicals	Surfactants	• Anionic Surfactants • Non-ionic Surfactants • Amphoteric Surfactants (Betaines)
Chemicals	Chlorine	• Chlorine • MCAA • Other Chlorine Downstream Products
Chemicals	Speciality Chemicals	• Phosphorus and Naphthalene Derivatives • Alkylphenols • Chemicals and Commodities Trading • Quartzite
Chemicals	Consumer Products	• Household and Industrial Cleaners, Detergents and Personal Care Products • Matches and Firelighters
Energy	Energy	• Renewable Energies • Conventional Energies
Logistics	Logistics	• Intermodal Transport • Road Haulage • Rail Transport
Holding	Holding	• Portfolio Management • Projects • Services

In accordance with our environmental concerns, this publication from the PCC Group was printed on Cocoon Silk - an ecological double-sided-coated matt paper. This paper is made of 100% waste paper via environment-friendly technology. The FSC® Certificate confirms that the raw materials used during the paper production process come from well-managed forests or other certified and controlled sources.

TEXT PAGES	
Brand	Cocoon Silk
Grammage	150
Number of pages	24

COVER PAGES	
Brand	Cocoon Silk
Grammage	250
Number of pages	4

PUBLICATION	
Size (cm)	21 x 29.7
Quantity	200

By using Cocoon Silk rather than non-recycled paper, the environmental impact was reduced by:

26 kg of landfill

3 kg CO_2 and greenhouse gases

35 km travel in the average European car

1 029 litres of water

57 kWh of energy

43 kg of wood

Carbon footprint data evaluated by Labelia Conseil in accordance with the Bilan Carbone® methodology. Calculations are based on a comparison between recycled paper used versus a virgin fibre paper - according to the latest European BREF data (virgin fibre paper) available.

PCC Group
Sienkiewicza 4
56-120 Brzeg Dolny, Poland
products@pcc.eu

Please visit our capital group business platform:
www.products.pcc.eu

PCC
More than Chemistry