IOI OLEOCHEMICAL

PHARMA

WITEPSOL® Hard Fats for

Suppositories & Ovules

IOI Oleo GmbH

CONTENTS

Packaging line

Hard facts about our hard fats

Since its first market introduction WITEPSOL® has become the synonym for hard fats and their use as drug delivery systems in ovules and suppositories.

With this legacy comes great responsibility that the employees of IOI Oleo are aspiring to meet and exceed on a daily basis.

Manufacturing takes place in a fully automated process, including pastillation and packaging line operating under clean room-condition.

This state-of-the-art production guarantees the highest possible standard, and in turn the quality of medicine in our ethical environment.

BASICS & ADVANTAGES OF RECTAL AND VAGINAL DRUG DELIVERY

Considerations:

- Localized and systemic drug delivery
- Avoidance of First-Pass Metabolism
- Fast on-set of drug release
- Reduced Systemic side-effects
- Robust & simple formulation concepts, only small number of excipients required

Patients Populations:

- Patients with gastrointestinal disorders
- Women`s Health
- Pediatric Patients
- Elderly Patients
- Emergency Medicine
- Nausea / Vomiting

Highest Quality & Compliance Standards 100 Years of Expertise in Lipids – Made in Germany

Our commitment and strict dedication to maximum product purity and safety are reflected in the daily efforts of our employees and our commitment to continuous improvement. The repeated certification of “Good Manufacturing Practice” (GMP) by the responsible German authority and the US FDA underline our claim to quality leadership.

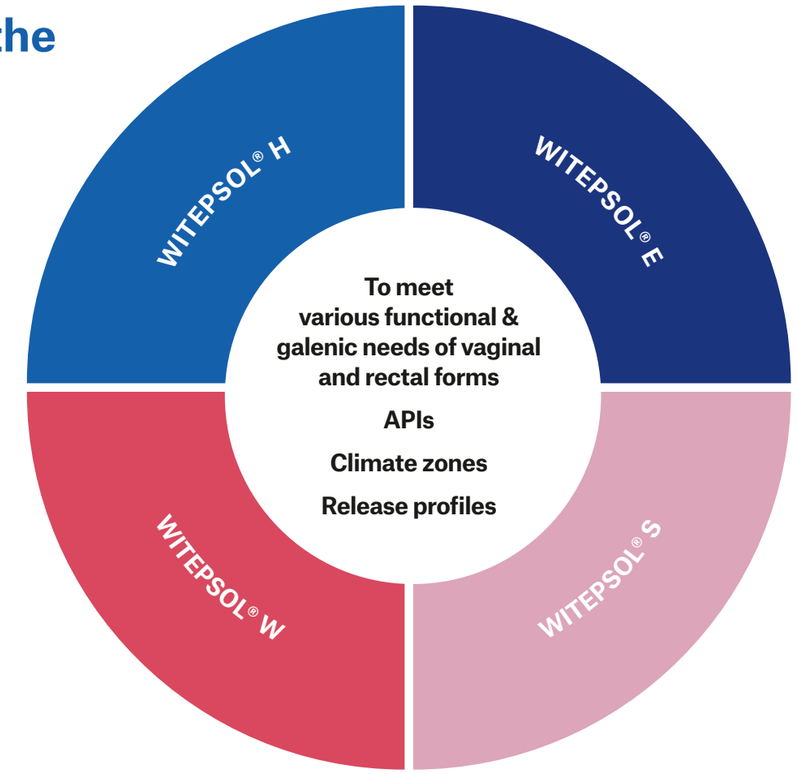
- ISO 9001 & ISO 45001
- EMAS
- RSPO SCCS
- EU GMP certified
- US FDA cGMP inspected
- HACCP
- Halal/Kosher

Product Range

Four WITEPSOL® Families provide selection and variety of properties to meet various functional & galenic needs for development and production vaginal and rectal dosage forms.

Selecting the right type

FOUR WITEPSOL® FAMILIES



17 SPECIALIZED WITEPSOL® GRADES – MAIN DIFFERENTIATORS

MELTING POINT

- The melting point of a formulated API / carrier system largely determines the release profile
- Ingredients in the formulation may influence melt characteristics by lowering or increasing melting point

HYDROXYL VALUE

- Most relevant to hydrophilic APIs that are dispersed or suspended in fat matrix
- Facilitates the absorption of APIs

ADDITIVES

- To modify & improve product or processing characteristics
- Surfactants, film formers, plasticizer
- Dispersibility/ Emulsification of certain API classes, wetting of mucous membranes, retention and absorption promotion

WITEPSOL® H

WITEPSOL® H hard fats are characterized by a low hydroxyl value

- Hydroxyl Values < 15, mainly triglycerides, very crystalline
- Very small gap between melting and solidification temps
- Recommended to process via cream melting (pre-crystallization)
- Most recommended for acidic API's e.g. ASA or Diclofenac
- H 19 contains Glyceryl Ricinoleate as additive

Compounds for suspension suppositories having a proportion of solid active compounds of less than 25%

WITEPSOL® H 35	melting point 33.5–35.5 °C	HV = max. 3
WITEPSOL® H 5	melting point 34.0–36.0 °C	HV = max. 5
WITEPSOL® H 15	melting point 33.5–35.5 °C	HV = 8-18

Compounds for suspension suppositories having a proportion of solid active compounds of over 25%

WITEPSOL® H 32	melting point 31.0–33.0 °C	HV = max. 3
WITEPSOL® H 12	melting point 32.0–33.5 °C	HV = 7-17
WITEPSOL® H 19	melting point 33.5–35.5 °C	HV = 20-30

Compounds for suspension suppositories and lipophilic active compounds; for melting point correction

WITEPSOL® H 37	melting point 36.0–38.0 °C	HV = max. 3

Looking for Hard Fats that are registered at Chinese National Medical Products Administration?

IOI Oleo has 12 WITEPSOL® grades registered! Send your inquiry to pharma@ioioleo.de!

WITEPSOL® W

WITEPSOL® W hard fats are characterized by a hydroxyl value from 20-50

- Contain higher amount of di- and monoglycerides than WITEPSOL® H
- Larger gap between melting and solidification temps, slower solidification
- More elastic, tolerant to shock cooling
- Slower sedimentation of suspended active particles
- Partial glyceride contents improves bioavailability of poorly soluble actives
- W 45 is the most hydrophilic compendial hard fat without additives, highest capacity to incorporate hydrophilic, polar actives

WITEPSOL® W 32	melting point 32.0–33.5 °C	HV = 40-50
WITEPSOL® W 25	melting point 33.5–35.5 °C	HV = 20-30
WITEPSOL® W 35	melting point 33.5–35.5 °C	HV = 39-49
WITEPSOL® W 45	melting point 33.5–35.5 °C	HV = 42-50

WITEPSOL® E

WITEPSOL® E hard fats having melting points above body temperature

- Mainly added for melting point increase/ adjustment:
  - Fat-soluble APIs decrease the melting point
  - Products for tropic climate regions
- WITEPSOL® E 75 with Bees wax additive

WITEPSOL® E 75	melting point approx. 38 °C	HV = max. 15
WITEPSOL® E 76	melting point 37.0–39.0 °C	HV = 30–40
WITEPSOL® E 85	melting point 42.0–44.0 °C	HV = 7–17

WITEPSOL® S for Women`s Health

VAGINAL OVULES: A GROWING THERAPEUTIC OPTION IN WOMEN'S HEALTH

The women's health market is experiencing significant growth, driven by increased awareness of female-specific conditions, a rising global middle class with greater access to care, and a shift toward personalized, wellness-oriented treatment strategies. Within this evolving landscape, vaginal ovules are gaining traction as a preferred delivery system for managing infections, hormonal imbalances, menopause-related symptoms, and intimate hygiene.

CLINICAL ADVANTAGES OF VAGINAL OVULES

- Targeted Delivery: Direct application to the vaginal mucosa ensures localized action with reduced systemic exposure.
- Enhanced Bioavailability: Bypasses hepatic first-pass metabolism, improving the efficacy of certain drugs.
- Patient Comfort: Soft, melt-in-body formulations reduce irritation and improve adherence.
- Broad Therapeutic Use: Suitable for antifungal, antibacterial, hormonal, and probiotic treatments.
- Discreet and Convenient: Easy self-administration with minimal disruption to daily life.
- Natural and Hormone-Free Options: Increasing availability of formulations with probiotics, herbal extracts, and other non-hormonal ingredients.
- Support for Menopausal and Microbiome Health: Effective in addressing vaginal dryness, pH imbalance, and biome restoration.

WITEPSOL® S

- More than just a hard fat, it's a drug delivery system
- First choice for vaginal route and rectal forms requiring better wetting of mucous membranes, enhanced dispersibility and absorption promotion
- Ethoxylated Cetostearyl alcohol Surfactant, enabling emulsion formation of aqueous & ethanolic extracts
- Glyceryl Ricinoleate: Wetting and gel formation, improving retention on mucous tissue
- Bees Wax: improves elastic properties and processability

WITEPSOL® S 51	melting point 30.0–32.0 °C	HV = 55–70
WITEPSOL® S 55	melting point 33.5–35.5 °C	HV = 50–65
WITEPSOL® S 58	melting point 31.5–33.0 °C	HV = 60–73

Additives	S51	S55	S58
Ethoxylated Fatty Alcohol	x	x	x
Glyceryl Ricinoleate	x		x
Bees Wax		x	

Hard fat recommendations for commonly used active pharmaceutical ingredients

WITEPSOL® H 15 / W 35
Actives for malaria treatment
Anesthetics
Anti-inflammatory substances
Antidepressants (alkaloids)
Antiemetics
Antiepileptics (barbiturates)
B vitamins
β-lactam antibiotics
Bronchodilatators
Expectorants
Male hormones
Nonsteroidal anti-inflammatory drugs
Steroidal antirheumatics (corticosteroids)

WITEPSOL® E 75 / E 85
Analgesics
Anesthetics
Antihypertonics
Steroidal antirheumatics (corticosteroids)

WITEPSOL® S 51 / S 58
Female hormones
Spermicides

WITEPSOL® W 45
Actives for hemorrhoidal treatment
Anti-inflammatory substances for treatment of Crohn´s disease and related indications Antimycotics
β-lactam antibiotics
Laxatives
Nonsteroidal anti-inflammatory drugs
Opioids such as Tramadol and related substances

Formulation Types

SOLUBLE API

API does not dissolve in carrier, remains as solid particle suspended in hard fat matrix

Active substances

Cannabinoids, Ibuprofen, Mesalazin partially, Cinchocain, Lidocaine

SUSPENSION

API is fat-soluble, typically affects physical properties of hard fat → Melt Viscosity & Melting point

Active substances

Paracetamol, Hormones, Urea, Lactic acid, Clindamycin, Econazole, Sertaconazole, Metronidazol, Nystatin, Benzalkonium Chloride, Lactobacillus, Bisacodyl, Codein, Zinkoxide, Diclofenac, Dimenhydrinate

EMULSION SUPPOSITORIES

API/ active content is liquid to semi-solid and not-soluble in hard fat → WITEPSOL® S types first recommendation

Active substances

Aqueous Extracts, ethanolic extracts e.g. Carraway, Hamamelis

Processing
Challenges in suppository production

CRACKS

Cracks (mostly longitudinal) are caused by stresses in the solid fat which arise from the different cooling rates at the exterior and within the mold. These visible damages can be avoided by

- selecting an elastic fat or
- lowering the casting temperature and increasing the cooling temperature, which makes the fat solidify more homogeneously.

Transverse cracks can also be caused by mechanical stressing of the solidifying suppository, for example in the sealing process, if the mold is filled excessively and pressure is applied to the compound.

DIMPLES, SINK HOLES

This fault in appearance occurs frequently and has the same causes as mentioned above: the fat in the center solidifies more slowly and draws, as a result of its contraction, material from above into the core.

MATT SURFACE

Fat bloom consists of crystalline fat formed by diffusion on the surface. If the gap between surface and packing film or foil is small (low contraction), this phenomenon – typical for fats – can usually not develop. It is therefore advantageous to use compounds showing low contraction or a process method using precrystallized fat (see above).

INHOMOGENEOUS DISTRIBUTION OF ACTIVE INGREDIENTS

If sedimentation of the active ingredient occurs despite stirring, the viscosity of the melt is usually too low. Reducing the temperature of the mixture or increasing the cooling after casting or adding viscosity enhancers (e. g. Aerosil) may solve the problem.

THICKENING OF THE MOLTEN MIXTURE

Some active ingredients can, in high doses, form gel-like masses with fat which do not solidify well. This phenomenon, which has not been fully explained, is probably caused by dissolution of the crystal surface by partial glycerides. Possible solutions are fatty bases having a low hydroxyl value, different particle size distributions of the active compound, or viscosity-lowering additives (e. g. lecithin).

POSTHARDENING

The melting point of cast suppositories can increase as a function of the fat type, the active ingredients, the method of production, and the storage conditions and time. The cause is a change in the crystal modification of the solid fat. The transition from the unstable α-modification which is predominant in the fresh state, to the stable β-modification proceeds via intermediate stages and can occur very slowly for example at low storage temperatures.

A stable end modification and a constant melting point can be achieved by applying a suitable tempering process during manufacturing. The cream melting process, long known in the preparation of pharmaceuticals, has not lost its significance in the industrial mass production of suppositories: the lowest possible casting temperature of the stirred compound and the highest possible cooling temperature are ideal. In this way, a high proportion of the stable end modification is produced from the beginning, and posthardening is thereby reduced.

Further reading

Recommended books with further references relating to pharmacological and technological aspects of rectal therapy:

[1] Nünberg, E. (Editor) “Hagers Handbuch der pharmazeutischen Praxis”, Band 2 “Methoden” [Hagers Handbook of Pharmaceutical Practice, Volume 2 “Methods”] Springer Verlag, Berlin, Heidelberg 1991

[2] Bosché, P.; Loth, H. “Solidification of Molten Hard Fats in Dependence on the Chemical Composition and Thermal Pretreatment“, [Die Pharmazeutische Industrie, EditioCantor Verlag, Pharm. Ind. 58, 2, 161–166 (1996)]

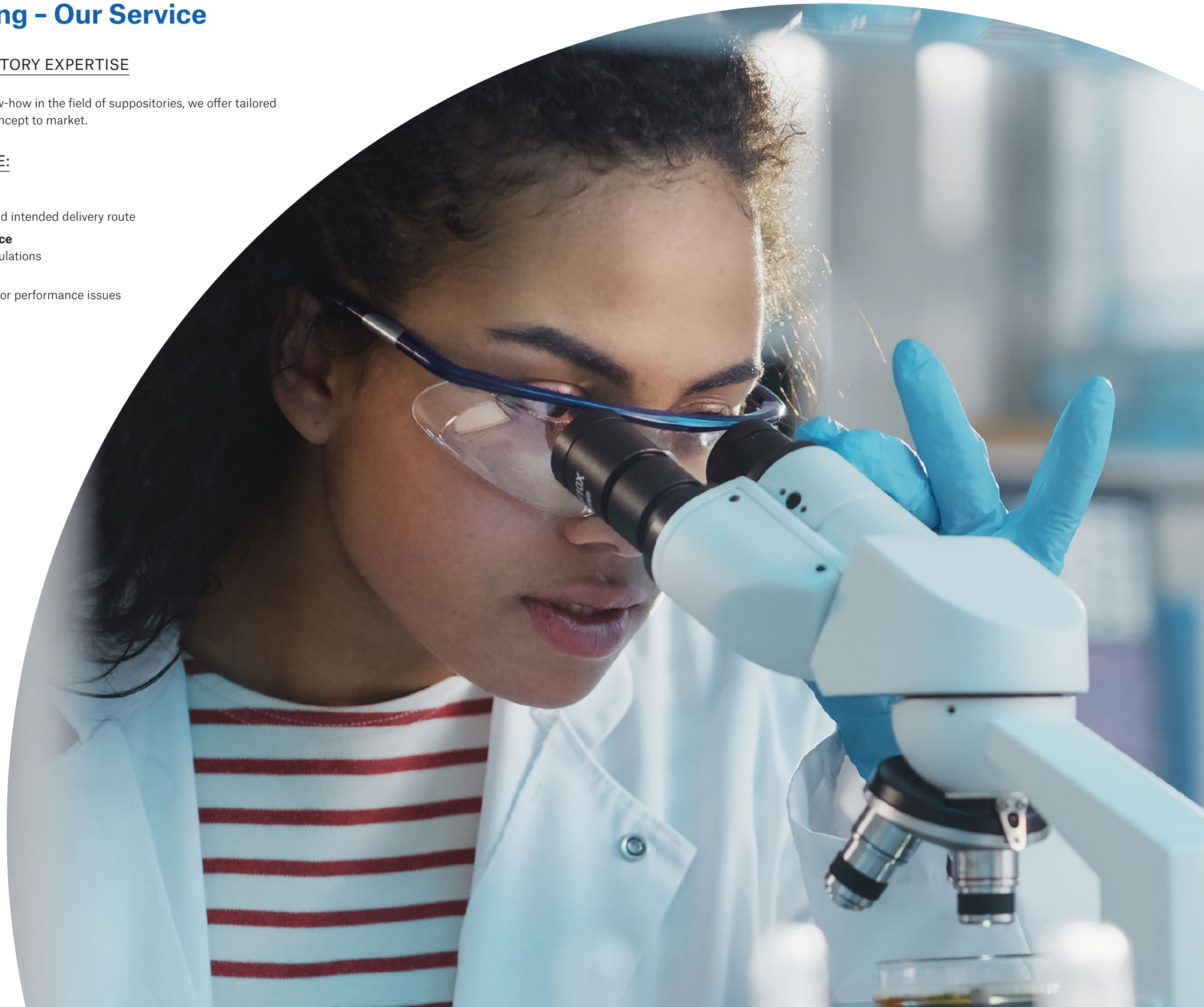
Application Engineering – Our Service

YOUR TRUSTED PARTNER IN SUPPOSITORY EXPERTISE

With decades of experience and deep technical know-how in the field of suppositories, we offer tailored support and solutions to help you succeed – from concept to market.

OUR SPECIALIZED SERVICES INCLUDE:

- **Product Recommendations**
  Based on active pharmaceutical ingredient (API) and intended delivery route
- **Formulation Adjustment & Re-Formulation Advice**
  Expert guidance to optimize or adapt existing formulations
- **Troubleshooting Assistance**
  Rapid problem-solving for formulation, processing, or performance issues
- **Direct Technical Coordination**
  With our Application Engineering team



Leading global expert and innovator of functionalised ester-based lipids with added value for pharma solutions.

IOI Oleo GmbH
Hamburg, Germany
+49 40 28 00 31-0
pharma@ioioleo.de
www.ioioleo.de

V2 2025