Kollicoat® MAE

Enteric coating.

BASF
The Chemical Company

MLW KommunikationsForm, Mannheim

The Preface

Kollicoat® MAE 30 DP and Kollicoat® MAE 100 P (methacrylic acid/ethyl acrylate copolymer) are "state of the art" film-forming agents for a reliable, convenient and cost-saving enteric coating of solid oral dosage forms.

Kollicoat® MAE provides an effective barrier to gastric juice which

- protects the stomach from drugs such as indomethacin, diclofenac or aspirin,
- protects acid-sensitive drugs, e. g. pancreatin from the contents of the stomach,
- increases the bioavailability of active ingredients so that high local drug concentrations are achieved in the small intestine increasing the bioavailability or
- releases the active ingredient, e. g. laxatives, at its site of action, the intestine.

Kollicoat® MAE 30 DP is an aqueous dispersion, Kollicoat® MAE 100 P the corresponding redispersable powder grade. Both products can be applied in aqueous spraying formulas and are not burdened with the disadvantages arising from organic solvents. Sub- and top coatings are normally unnecessary. Kollicoat® MAE 100 P can also be sprayed from organic solvents if required.
Tablets coated even with small amounts of Kollicoat® MAE withstand gastric juices as well as rigours of handling, packing and storage, exhibiting stable enteric release profiles.
Production times with aqueous Kollicoat® MAE 30 DP are comparatively short, leading to reduced manufacturing costs.
When exposure to extreme climatic conditions (frost or temperatures > 30°C) cannot be excluded during transport or storage, the redispersable powder Kollicoat® MAE 100 P is the enteric coating material to choose.

The Product

Product forms:
Kollicoat® MAE 30 DP is marketed as an aqueous dispersion with a solids content of 30 %. The milky white, low-viscosity product has a faint, characteristic odour.

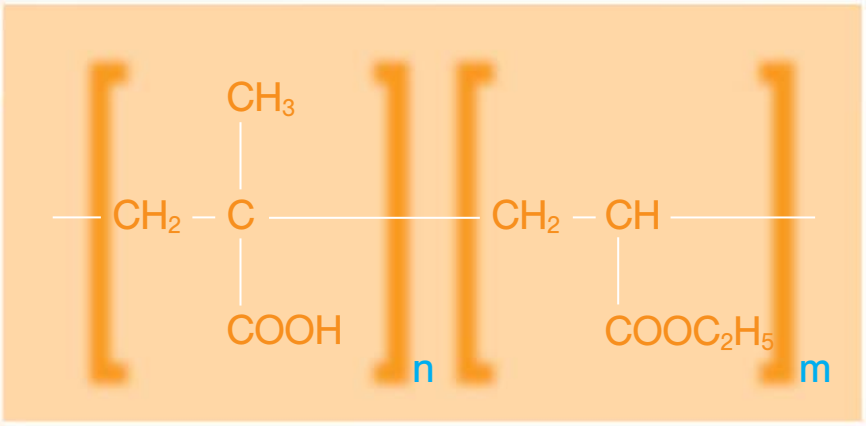
The dispersion contains 0.7 % sodium lauryl sulfate (USP) and 2.3 % Polysorbate 80 (Ph. Eur.) as emulsifying agents. The percentages in each case refer to the solids content.

Kollicoat® MAE 100 P is a white, redispersable powder, originating from the Kollicoat® MAE 30 DP dispersion. Prior to spray drying the dispersion is partially neutralized with NaOH. This eases redispersion for the final formulation of the spray suspension. The product consists of 95.8 % copolymer, max. 2.3 % Polysorbate 80 (Ph. Eur.) and max. 0.7 % sodium lauryl sulfate (USP). About 1.2 % sodium hydroxide was applied for neutralisation.

Both Kollicoat® MAE grades are weakly acidic and dissolve at a pH above 5.5.

Trivial names:
Methacrylic Acid Copolymer Dispersion (USP-NF), Methacrylic Acid Copolymer LD (JPE), and Methacrylic Acid-Ethyl Acrylate Copolymer (Ph. Eur.).

Pharmacopoeia:
Kollicoat® MAE 30 DP complies with the requirements of the European Pharmacopoeia monograph “Polyacrylate dispersion 30 %”, the USP-NF monograph “Methacrylic Acid Copolymer Dispersion” and the JPE monograph “Methacrylic Acid Copolymer LD”.



Structural formula:
Kollicoat® MAE grades are copolymers derived from methacrylic acid/ethyl acrylate.

The ratio of the components in the copolymer is roughly 1:1. The average molecular weight is in the order of 250,000.

The Application

Tablet-coating made simple.

Kollicoat® MAE can be applied as enteric coating to all conventional solid oral dosage forms, e. g. tablets, capsules, pellets and granules. The normal amount of polymer applied is 4–6 mg per cm^2 of tablet surface, or 10 to 30 % by weight on particles such as pellets, granules or crystals with sizes in the range of about 0.5 to 3.0 mm.

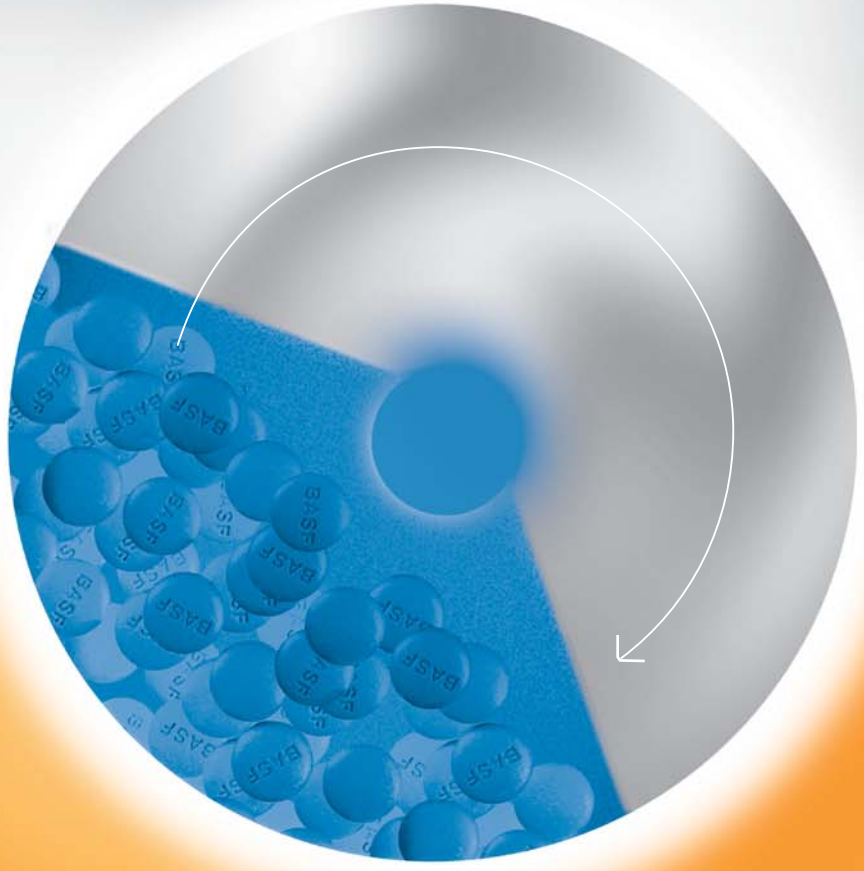
Kollicoat® MAE applied in low coating levels, 0.5–2.0 mg/cm^2 solids, can be used for the following purposes:

- Masking unpleasant tastes and odours
- Protecting incompatible active substances
- Protection against atmospheric humidity (short-term)

Kollicoat® MAE applied in high coating levels, e. g. 10 to 20 mg/cm^2 is able to protect drugs during long-term storage against humidity. Even hygroscopic drugs or drugs sensitive to hydrolysis can be coated with this aqueous dispersion by using a reduced spraying rate at the beginning of the coating process.

In combination with sustained release polymers Kollicoat® MAE slows down a too quick release of active material in the initial phase of dissolution.

Kollicoat® MAE 30 DP and Kollicoat® MAE 100 P can be processed as aqueous polymer dispersions in all film-coating or fluidised-bed equipment that is commonly used in the pharmaceutical industry. Kollicoat® MAE 100 P can also be sprayed from organic solution. Perforated coating pans are particularly suitable for tablets whereas fluid-bed coaters are preferred for small particles that have a stronger tendency to agglomerate.



Perforated pan coater

Instructions for processing:

It is essential to add plasticizer to improve the flexibility of the films. Suitable plasticizers or gloss intensifiers are

- 1.2-Propylene glycol
- Triethyl citrate
- Polyethylene glycols and
- Triacetin

Spray suspensions with a 15–30 % solids content give good results and the shortest spraying times.

The following recommendations are made to avoid problems in incorporating excipients in the aqueous suspensions:

- Dilute the dispersion to a solids content of 20 %
- Stir the desired excipient in the form of a dilute solution or suspension into the dispersion.

The direct addition of pure plasticizer or pigments to the undiluted film-former can cause coagulation.

The following excipients can be used in formulas with Kollicoat® MAE grades:

Release and smoothing agents

- Talc
- Syloid
- Aerosil
- Kaolin

Colorants for the film coatings

- Titanium dioxide
- Colored pigments (e. g. iron oxides)

The polymer in these Kollicoat® MAE products has a high pigment binding capacity, with the result that up to twice the amount of pigments or other excipients may be added.

Stabilizing agents

(usually not necessary)

- Nonionic emulsifiers, e. g.
- Cremophor® RH 40
- Lutrol® F68

Antifoaming agents

(usually not necessary)

- Simethicone

The recommended addition rate of plasticizer is 10–25 %, referred to the dry polymer. 1.2-propylene glycol improves the processability and enteric resistance of the film coatings and should be the preferred plasticizer. Triethyl citrate also exhibits good properties with regard to the resistance against gastric juice.

Fluid bed coater

The Example

Colored enteric film coating based on Kollicoat® MAE 30 DP

Composition of the spray suspension:

The formula for 5 kg of cores (diameter 9 mm; weight 330 mg):

	Parts by weight [g]	% composition
Coating suspension		
Kollicoat® MAE 30 DP	600	50.0
Propylene glycol	27	2.3
Water	393	32.7
Pigment suspension		
Iron oxide red 30	6	0.5
Titanium dioxide	6	0.5
Talc	48	4.0
Water	120	10.0
	1,200	100.0

Solids content of the spray suspension: 22.3 %
Content of polymer (solids): 15.0 %
Polymer applied: 4.8 mg/cm²
Total solids applied: 7.0 mg/cm²

Coating pan	Accela Cota
Size of batch	5 kg
Inlet air temperature	60 °C/140 °F
Product temperature	30–35 °C/86–95 °F
Rate of spraying	40 g/min
Time of spraying	30 min
Pressure	2–3 bar

Machine parameters:

The spraying trials were performed in a Manesty 24" Accela Cota coating pan.

The Example

Colored enteric film coating based on Kollicoat® MAE 30 DP/100 P

Preparation of the spray suspension with Kollicoat® MAE 30 DP:

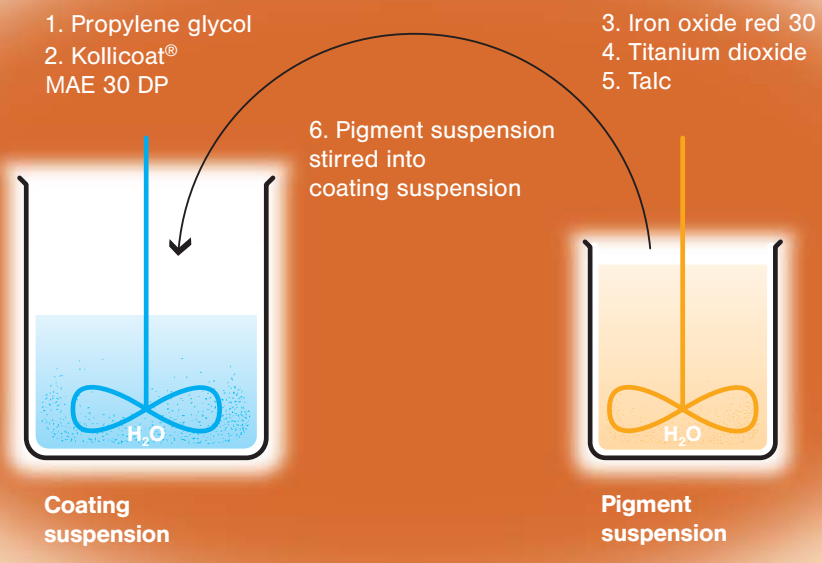
- Coating suspension.
  Propylene glycol is first stirred into the given amount of water. Then Kollicoat® MAE 30 DP is stirred in.
- Pigment suspension.
  Iron oxide red 30, titanium dioxide, and talc are intensively stirred in water and homogenized (corundum disk mill or Ultra Turrax).
- Spray suspension.
  The pigment suspension is stirred into the coating suspension. It is recommended to stir the spray suspension during spraying in order to avoid sedimentation.

Preparation of the spray suspension with Kollicoat® MAE 100 P:

- Coating suspension.
  Kollicoat® MAE 100 P is carefully stirred into the given amount of water. The stirrer speed is adapted to the viscosity from time to time avoiding foam production. To complete the redispersion the system is stirred for 3 to 4 hours. Finally the plasticizer is added.
- Pigment suspension.
  Iron oxide red 30, titanium dioxide, and talc are intensively stirred in water and homogenized (corundum disk mill or Ultra Turrax).
- Spray suspension.
  The pigment suspension is stirred into the coating suspension. It is recommended to stir the spray suspension during spraying in order to avoid sedimentation.

Coating suspension + Pigment suspension = Spray suspension

(Please find further formulations in our “Technical Information – Kollicoat® MAE grades”)



The Example

Colored enteric film coating based on Kollicoat® MAE 100 P

Composition of the spray suspension:

The formula has been calculated for 500 g of crystals (diameter 0.3–1.0 mm):

	Parts by weight [g]	% composition
Polymer suspension		
Kollicoat® MAE 100 P	75.0	15.0
Propylene glycol	11.3	2.25
Water	336.2	67.25
Pigment suspension		
Titanium dioxide	2.5	0.5
Iron oxide red 30	2.5	0.5
Talc	20.0	4.0
Water	52.5	10.5
	500.0	100.0

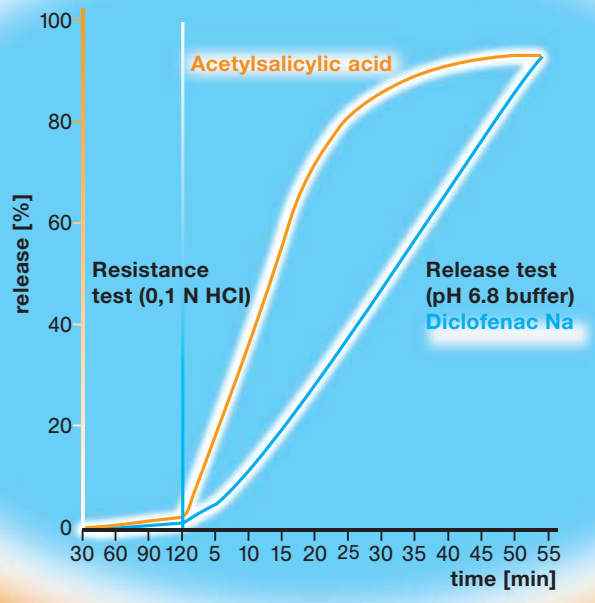
Solids content of the spray suspension: 22.25 %
Solid polymer in the spray suspension: 15.0 %
Solid polymer applied: 4.0 mg/cm²
Total solids applied: 5.9 mg/cm²

Coating equipment	WSG Aeromatic Strea 1
Size of batch	500 g
Air supply temperature	60 °C/140 °F
Exhaust air temperature	35 °C/95 °F
Spraying pressure	2–3 bar
Time of spraying	100 min

Machine parameters:

The spraying trials were performed in a WSG Aeromatic Strea 1 fluidised bed granulator.

Release rates of diclofenac Na pellets and acetylsalicylic acid crystals.



The Coating Process

In a comparative study* different materials for enteric coating were investigated:

Hydroxypropyl methylcellulose acetate succinate (HPMCAS), 2 different hydroxypropyl methylcellulose phthalate (HPMCP) products, cellulose acetate phthalate (CAP) and methacrylic acid/ethyl acrylate copolymer 1:1 (Kollicoat® MAE).

CAP aqueous	Kollicoat® MAE aqueous	HPMCP aqueous	HPMCP organic	HPMCAS aqueous	Ingredients [%]
11.04	15.00	9.70	5.00	7.00	Film-former
		1.80			Ammonia (30%)
			79.19		Ethanol
	0.50				Kollidon® 30
				0.21	Sodium lauryl sulfate
0.26	0.50	0.33	0.17	0.24	Iron oxide red
	2.00	2.50	1.50	2.10	Talc
0.26	0.50	0.33	0.17	0.24	Titanium dioxide
3.35		1.00			Triacetin
	1.50			1.96	Triethyl citrate
0.10					Tween 80
84.99	80.00	84.34	13.97	88.25	Water

Composition of the spray dispersions according to technical data sheets.

CAP aqueous	Kollicoat® MAE aqueous	HPMCP aqueous	HPMCP organic	HPMCAS aqueous	Process Parameter
78	50	70	60	70	Inlet air temperature [°C]
32–33	35–38	32	36	33–35	Product temperature [°C]
60	30	30	60	40	Rate of spraying [g/min]
	5 minutes at 50 °C				Drying
60/60	No heat treatment			30/60	Heat treatment [min/°C]

Process parameters in coating and subsequent treatment according to technical data sheets.

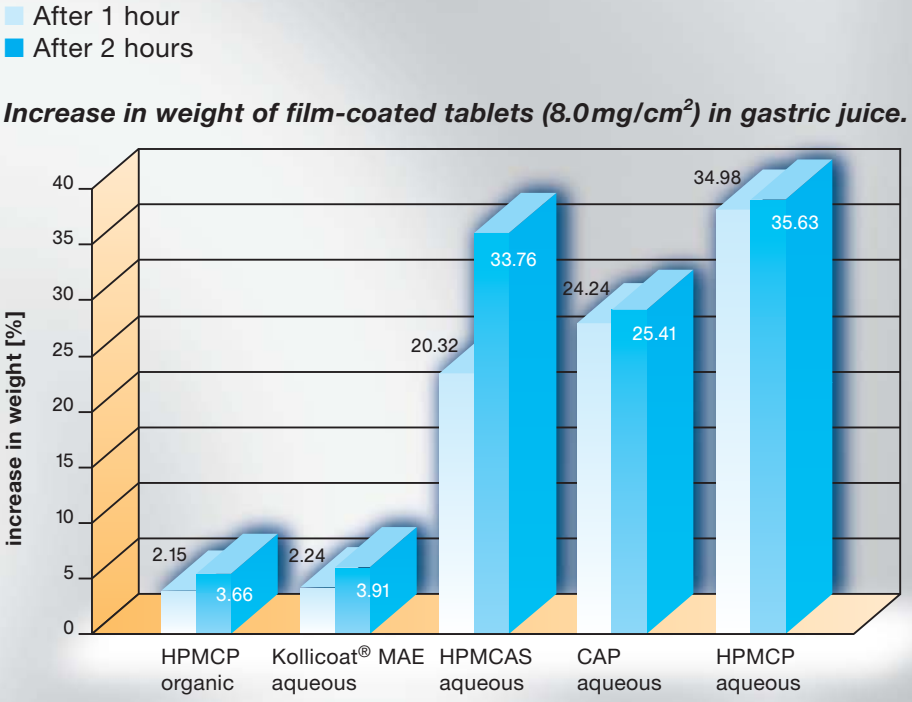
Caffeine cores were coated in an Accela Cota 24".
The composition of the spray suspensions and solutions, the method of preparation and the process parameters were taken from the respective manufacturer's technical data sheets.

One of the HPMCP products was sprayed in an organic solvent, all others in aqueous medium.

* K. Kolter, S. Scheiffele, G. Schepky
KOLLICOAT MAE – EFFECTIVENESS AND ECONOMY IN ENTERIC COATING
Proc. 2nd World Meeting APGI/APV, Paris, 25/28 May 1998

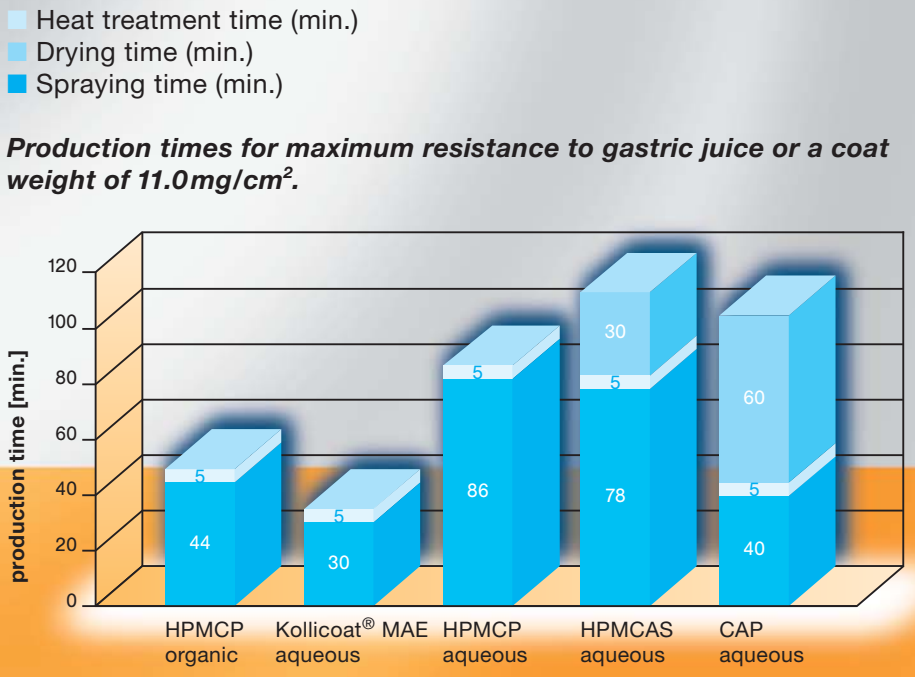
The Result

The acid permeation results show that to achieve resistance to gastric juice, different minimum film thicknesses are required for each film-forming agent. To achieve adequate resistance towards gastric juice, a coating of only 5.5 mg/cm² is required with Kollicoat®, which is just as little as with the HPMCP product in an organic solution. Taking into account the different coating weights required to achieve good resistance to gastric juice the production times are as shown below.



Increase in weight of film-coated tablets (8.0mg/cm²) in gastric juice.

The degree of resistance to gastric juice was determined from the increase in weight of film-coated tablets during resistance test.



Production times for maximum resistance to gastric juice or a coat weight of 11.0mg/cm².

The different processing times in the preparation of spray suspensions are not taken into account here. More time and effort are always required to prepare suspensions from powders than to mix in an aqueous dispersion such as Kollicoat® MAE. Furthermore unlike the cellulose derivatives, which undergo degradation to release phthalic acid, succinic acid and/or acetic acid, Kollicoat® MAE is highly stable against hydrolysis.

The Summary

Kollicoat® MAE 30 DP and Kollicoat® MAE 100 P are first choice enteric coating agents which

- allow an easy preparation of the spray suspension
- shorten the coating process as the concentration of the film-former in the spray suspension is high and the amount of film-former needed is little
- form films with a smooth shiny surface, even when mixed with large quantities of pigments
- provide reliable and highly stable resistance to gastric juice
- are purely aqueous dispersions and not burdened with the disadvantages of organic solvents

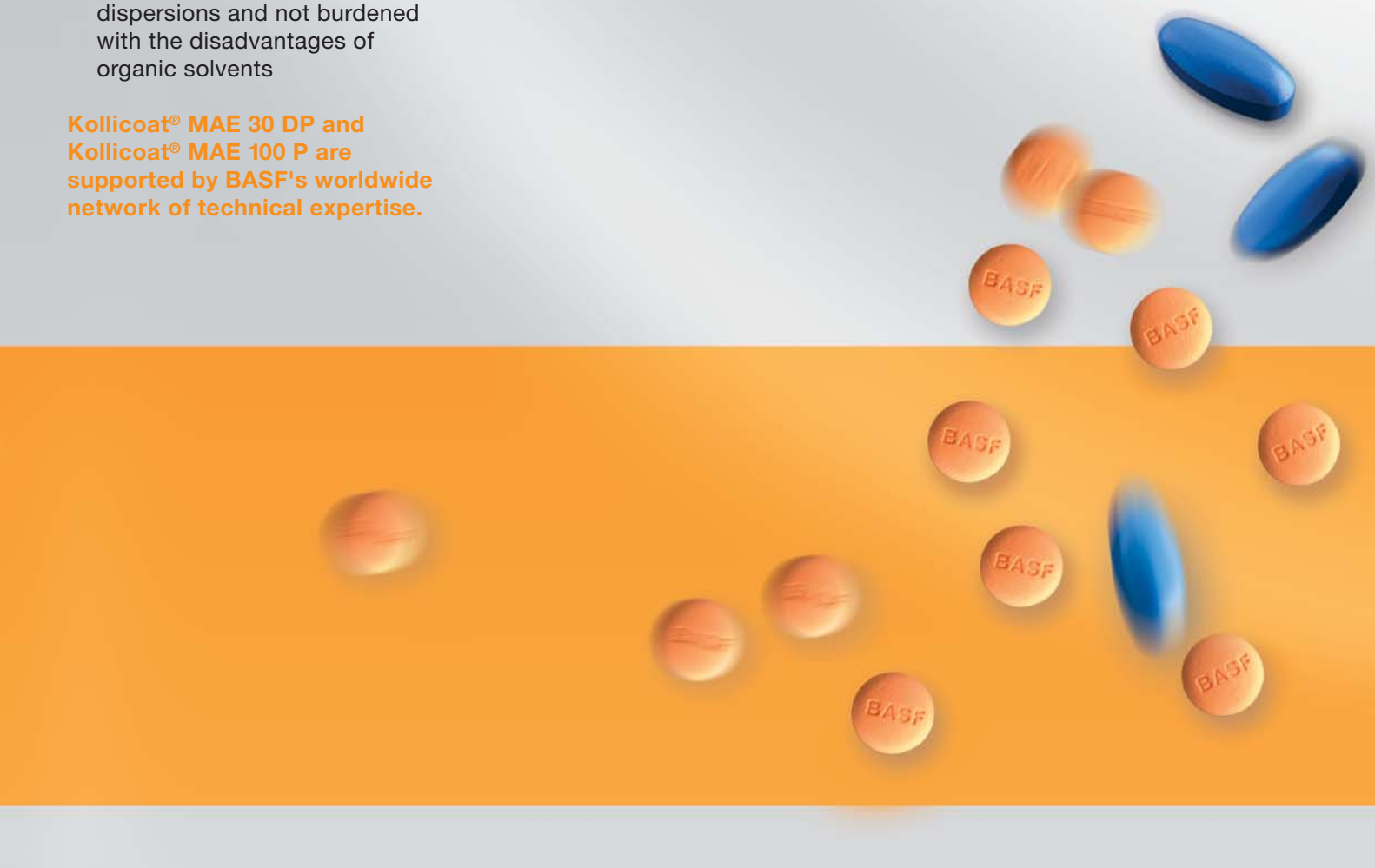
Kollicoat® MAE 30 DP and Kollicoat® MAE 100 P are supported by BASF's worldwide network of technical expertise.

The major advantages of the product are:

- Batch size of ca. 26 MT results in reduced analysis costs (advantage ~0.20 EUR/kg)
- Better gastric resistance than cellulose derivatives
- Identical to market leader Eudragit L 30 D-55

- Kollicoat® MAE 100 P is partly neutralized and thus no caustic soda is to be handled in production
- Better gastric resistance than cellulose derivatives
- Same chemistry as market leader Eudragit L 100-55, but already neutralized

Kollicoat® MAE produces enteric coatings of excellent quality more easily and at lower cost than film-forming agents based on cellulose derivatives.



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Please send the following information.

- Technical information on Kollicoat® MAE grades.
- Sample of Kollicoat® MAE 30 DP 0.5 kg.
- Sample of Kollicoat® MAE 100 P 0.5 kg.
- **Please contact me, I would like to know more about Kollicoat® MAE.**
- Technical information on Kollicoat® IR White.
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- “What’s Your Coat Name?” CD-ROM.
- Newsletter “ExAct” (Excipients & Actives for Pharma).

Local contact:

or Headquarter Germany:

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