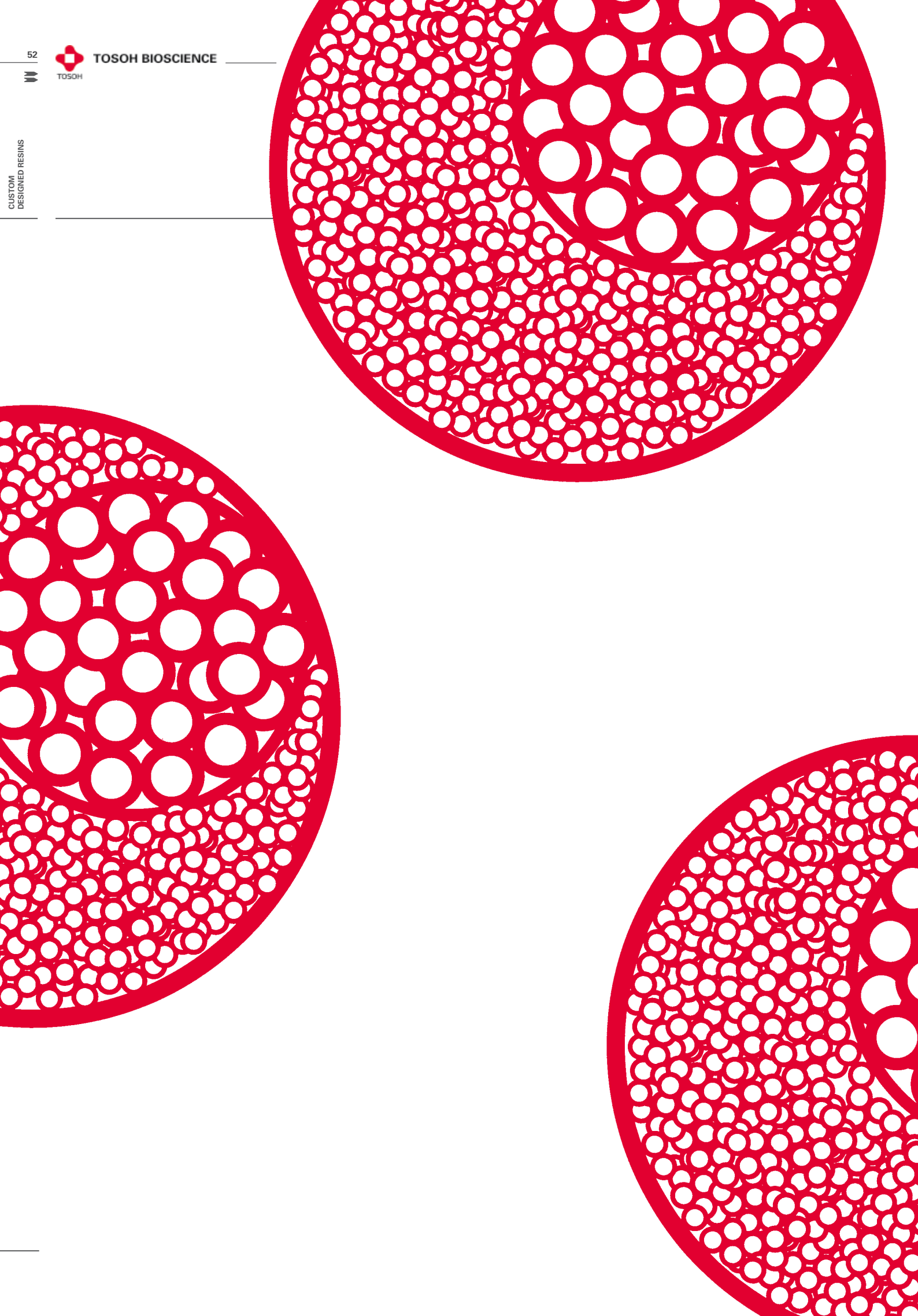




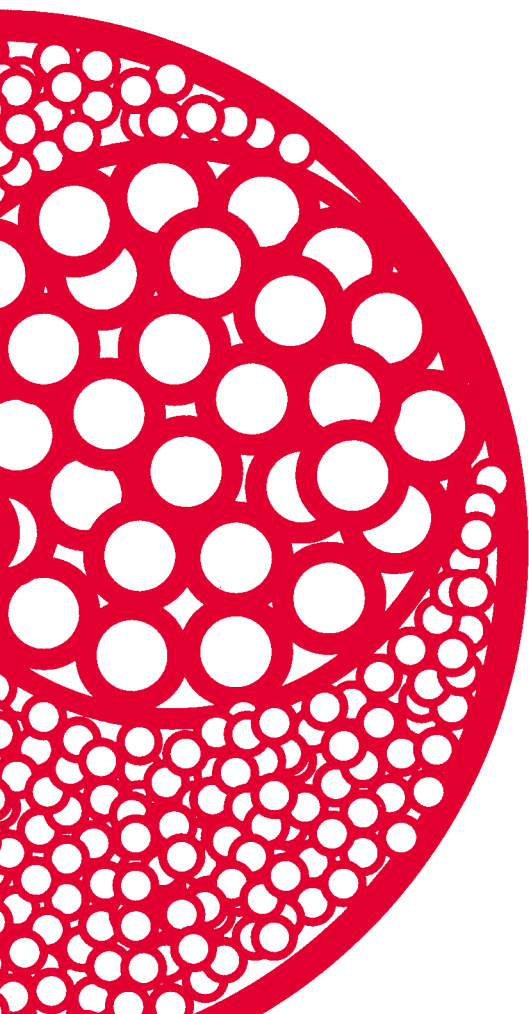
TOSOH



CUSTOM DESIGNED RESINS

CUSTOM RESINS

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TOSOH FACT

Tosoh Bioscience provides solutions for today's biological purification needs. In fact, some of the first commercial HIC products were manufactured by Tosoh. We take pride in our ability to design new products based on existing chemistries to solve specific customer applications.

We encourage you to have a confidential discussion with us about your specific needs. Whether it is a surface modification of an existing product or the creation of a new one, we encourage you to call on us to meet your needs for a customized solution.



CUSTOM DESIGNED RESINS

OVERVIEW

Occasionally special purification needs require special adaptations to existing chromatographic resins for optimized operation of your process. This section explains in general terms Tosoh's custom resin development procedure.

TOSOH'S RESIN INNOVATION PROGRAM (TRIP)

Tosoh Corporation of Japan has introduced a new resin innovation program. Ideal candidates for this program are drug targets that have been selected for clinical trials which, if successful in the clinic, will be commercially manufactured. This program is not available for early stage laboratory research or the isolation of small amounts of new therapeutic proteins.

NEW PROJECT APPROVAL FOR TRIP

To receive a "Go" status for TRIP some evaluation is needed. During preliminary discussions, prior to the generation of scouting samples, an assessment is made of whether the project fits into Tosoh's scaffolding capabilities. If a fit is established, the projected liter volume for the new resin is reviewed. Decisions are based on the quantity projected for use after therapeutic approval and launch, but for high value added resins, projected commercial liter volumes of less than 100 liters have been approved.

NEW RESIN DEVELOPMENT TIME LINE

Tosoh Bioscience and Tosoh Corporation of Japan have the resources to develop custom resin products. The custom resin optimization timeline closely mirrors a customer's need to produce products for clinical trials. Only with detailed sample evaluation data from the customer, chemistry optimization and manufacturing lot release criteria can be established by Tosoh so a close cooperation between the customer and Tosoh is crucial.

TABLE 1

TRADITIONAL CHROMATOGRAPHIC LIGANDS

Anion Exchangers	Diethylaminoethyl (DEAE) Quaternary Anion Exchanger (QAE)
Cation Exchangers	Sulfopropyl (SP) Carboxymethyl (CM) Sulfonic Acid (S)
Hydrophobic Interaction	Hexyl Butyl Phenyl Polypropylene glycol (PPG) Ether

TABLE 2

TOSOH METHACRYLIC BASE BEADS USED FOR SEC

Pore size (Å)	50	125	400-500	750	1000	>1000	>1700
Product name							
Toyopearl HW-Type	40	50	55	60	65	75	80
TSKgel PW-Type	G1000	G2000	G4000		G5000	G6000	

TABLE 3

AVAILABLE PARTICLE AND PORE SIZE COMBINATIONS

Pore Diameter (angstroms)	Particle Size (microns)							
	200	100	75	65	35	30	20	15
>1700		★						
>1200	★	★						
1000		★		★	★	★	★	★
750		★	★	★				
400-500	★	★		★	★	★	★	★
125				★	★			
50	★	★		★	★			

7 x 8 = 56 possible combinations

CUSTOM DESIGNED RESINS



RESIN OPTIMIZATION (SEMI-CUSTOM COMMERCIAL RESINS)

In many cases the optimization of an already commercial resin can be accomplished by a more judicious selection of particle size, pore size, and currently available ligands (Table I). See the various combinations of these physical parameters in the Toyopearl SEC section of this catalog. When these products are combined with the comparable polymer chemistry TSKgel PW products (Table II), there are 49 different combinations (Table III) to act as a scaffold for an improved resin product. All kinds of modes can be optimized.

CUSTOM RESINS

In more difficult situations custom resins can be developed for a customer. Ligand screening, selection, density, length of spacer arm, degree of crosslinking and degree of grafting all add to the fundamental scaffold of the semi-custom resins. The objective in designing a certain resin is to develop a bead that has maximum accessible surface area with an optimized ligand density using an appropriate spacer arm which fits the conformational attachment requirements of the target. These parameters can have a dramatic effect on the resin's chromatographic and economic performance.

GETTING STARTED

To initiate the TRIP program contact your local Business Development Manager. A period of due diligence will be started where the appropriate information can be exchanged in confidence between us. Detailed communications on these topics requires an in effect two way Confidential Information Disclosure Agreement between Tosoh Bioscience GmbH and the customer. If the project looks promising to both parties several laboratory scouting samples will be prepared and sent to the customer site for evaluation.

COMMERCIALIZATION

Once a "Go" decision is made, the performance specifications are determined from the optimized scouting samples, the custom resin enters into Tosoh's "ISO 9001" product commercialization process. Several small manufacturing batches are then made to set lot release criteria. Regulatory support studies are initiated at this time.