



TOSOH THE CUSTOMER MAGAZINE

CORONA/CHALLENGE/CONFIDENCE

NO. #01
2020



TOSOH BIOSCIENCE

02 EDITORIAL DEAR READER

Welcome to the first issue of the Tosoh Bioscience customer magazine in 2020. Initially, this magazine was supposed to be the Analytica 2020 issue. Then SARS-CoV-2 reached Europe, Analytica 2020 was postponed, and today, the Corona pandemic keeps the whole world in suspense.

We have hesitated to devote an entire issue of the journal to this topic, but on the other hand most other topics seem to be less relevant compared to Corona. Rather than submitting to the dictates of the virus, we decided to highlight the leaps in science and digitalization, as well as the opportunities for life as such that are emerging in these extraordinary times.

STAY HEALTHY AND ENJOY READING.....

REGINA ROEMLING | SENIOR MARKETING MANAGER
TOSOH BIOSCIENCE GMBH

SUPER T, HIS FRIENDS AND THE NEW CORONA RULES



OR CHECK IT HERE:
<https://youtu.be/VXtwjPxJn1l>

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➤ IMPRESSUM

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03 TOSOH AND THE PANDEMIC

RELIABLE SUPPLY AND SUPPORT UNDER THE COVID-19 RESTRICTIONS

For decades, Tosoh Bioscience has enabled its biopharma partners to provide robust diagnostics solutions and safe and efficient therapies for life-threatening diseases. During the on-going battle against COVID-19, the necessary steps have been taken to ensure business continuity and to support the various R&D and production activities to combat the new Corona Virus. Our utmost priority is to ensure the health and well-being of our employees so we can continue to serve our customers and the life sciences community.

In the diagnostics field, Tosoh is developing solutions for both detecting the SARS-CoV-2 RNA during acute infections and detecting antibodies specific to SARS-CoV-2 through serological tests in patients who symptomatically or asymptotically contracted SARS-CoV-2. Tosoh Bioscience's chromatography experts are focusing their technological leadership on chromatography materials to support the development of methods for the analysis and industrial production of therapies, vaccines, and diagnostic solutions at their biotech and pharma customers.

As COVID-19 continues to profoundly impact the lives and operations of our customers, communities and employees, Tosoh Bioscience has taken the necessary steps to ensure business continuity for our customers. We certainly understand the need for our Process Media, U/HPLC Columns, and GPC systems and detectors in many essential life sciences and biotechnology manufacturing and are committed to deliver these products to our customers.

Currently, our manufacturing and supply chain operations continue functioning as normal. We are working diligently with suppliers of raw materials and shipping partners to mitigate any potential manufacturing and/or shipping interruption(s) and to ensure continuity and availability of our products. Moreover, in preparation for any unforeseen circumstances, Tosoh Bioscience has increased inventory levels in EMEA.

We have introduced a virtual workplace for most of our staff in the hard-hit areas, while maintaining critical employees to operate manufacturing and supply chain operations. In addition, we have elevated internal safety precautions and hygiene across global offices, warehouses and production sites to further prevent the transmission of COVID-19.

Our Sales and Technical Support teams are working remotely and are able to easily interact via virtual platforms to answer any inquiries and provide support and training. Customer service representatives are available within office hours to answer questions regarding orders and deliveries. During the first week of May, we met for our first three day Sales & Tech Meeting in 2020 – for the first time virtually.

04 PEOPLE BEHIND TOSOH

IMPRESSIONS OF THE CORONA LOCKDOWN FROM ALL OVER THE WORLD

AS COVID-19 IS INFLUENCING AND CHANGING WORK AND PRIVATE LIVES ALL OVER THE GLOBE, WE ASKED OUR COLLEAGUES ABOUT THEIR COVID-19 EXPERIENCES. WE WERE IMPRESSED HOW POSITIVELY AND STRONGLY OUR COLLEAGUES MET THE CHALLENGES.

The measures taken for lockdown varied from country to country. In the U.K., the authorities only advised sanitary measures in the initial weeks. As infections grew a partial stay-home order was enforced. There were exceptions for work travel, where home working was not possible, essentials-only shopping, and one-hour exercise. In Belgium, where our supply chain and other shared services are located, there was a "lockdown light" similar to the one in Germany. You could go outside for walking or cycling and you could do urgent trips such as to a supermarket or pharmacy. It was not allowed to walk or sit together with more than three people, who do not live in one household. Non-essential shops, restaurants and bars were closed. France, Spain and Italy imposed real confinements where you had to present a permission to leave your home.

Bernd, Germany: "The discipline in most European countries was impressive. Especially in Germany we were lucky to limit the infections and we realized the high quality of our health system."

Our colleague Ms. Yan Zhang from China reported: "In order to reduce the risk of infection, we were kept at home following national policies, where we read the news every hour, and our anxiety increased exponentially. At the peak time, large numbers of people died every day, nearby shops were closed, and well-wowed companies went out of business."

Michael, Germany: "It is amazing to see how intense our customers are involved in COVID-19 related R&D activities. The number of lab workers is reduced, nevertheless we receive a lot of requests for our products. It makes me proud to be responsible for products which (hopefully) can be used to defend the COVID-19 attack."

Ute, Germany "What impressed me most happened in my private life: the degree of solidarity and anticipation I observed. Some people started groups to create networks to help people in need. Those people anticipated the needs that would arise and found ways to reach people without internet access or the like."

Of course the scale of this pandemic and the implications for everyone were scaring. And the fact that nobody knows what will come, and when it will end. The uncertainty has naturally frightened many colleagues but it turned out that the work routines did not change that much for those working in administration, accounting, or marketing. Most of them work from home for the time being - applause for our IT colleagues to make this possible on very short notice - with the positive side effect that they save a lot of time that they would otherwise need for commuting to work. However, many stated that they miss personal meeting with their colleagues.

Alex, U.K.: "On a team level, it was incredulous how our team worked seamlessly despite the odds. We responded to enquiries faster and collaborated using the company's internet voice protocols – cheaper and robust in business environment."

Change in daily routines was of course more profound in the sales and field service engineers teams. In contrast to many other industries, most sales colleagues experienced that they have as much work as before and that some additional new and COVID-19 related projects have come up. Alex (U.K.) stated: "Most importantly, my face-to-face meetings with customers ceased. Scheduled meetings were cancelled. Online teleconferences became the new normal."

Bea, Belgium: "We have seen now we don't really need a lot of things to survive, I hope people don't forget that again. What we really need is a world in which we can live and in which the environment is not destroyed."

05 PEOPLE BEHIND TOSOH

The positive effects of the lockdown were mostly related to private life. Many colleagues enjoyed a better work/life balance. As weekend plans disappeared there was some extra time used to rediscover old hobbies or walk the dog more than ever. In addition we learned to value simple things such as visiting the grandmother or godchild and we experienced that these are the things that really matter. For Peter (Belgium) the home office brought a very special adventure: "Last week, a new lamb was born. Working from home was practical as I could check the lamb every 4 hours." Positive effects that Bea from Belgium noticed were: "Somehow the people are friendlier. There is more time for the things that really matter. The spontaneous solidarity actions, a 'wir schaffen das' (we can make it) feeling among the people. The creativity of many people." The positive effect on the environment was also very obvious. We received a lot of feedback about things one can be proud of or that were particularly impressive during this period (see highlighted citations).

Yan Zhang, China: "It also shows that with the development of science and technology, much work can be done through the Internet. In the era of efficiency, smart human beings can fight against the virus, but also continue to maintain the efficient operation of the earth."

Peter, Belgium: "I think in general that we can be proud of how everybody within our company is handling this special situation." "The impact on the environment is impressive, especially the satellite images from Wuhan and Lombardy showed that the air pollution almost disappeared above these regions".

In the long run, many are afraid that the positive effect on the environment will disappear as soon as the economy revives and that it might even get worse if certain industries will try to recover from the lockdown as soon as possible at all costs regardless of their impact on the environment. But many also hope for positive long-term effects: Working from home might be adopted by many companies and remote working and video conferencing will play a much greater role. This will boost digitalization and funding for it. Our answers to this crisis might direct towards more solidarity and towards a more sustainable society in which activities beneficial for the common good are prioritized.



06 WHAT'S NEW PRE-PACKED COLUMNS

SPEED UP THE DEVELOPMENT AND REDUCE DSP COSTS OF BIOTHERAPEUTICS

THE ON-GOING RACE AGAINST THE CORONA VIRUS MAKES IT MORE EVIDENT THAN EVER: SCIENTISTS NEED TO DEVELOP BIOTHERAPEUTICS, VACCINES, AND DIAGNOSTIC SOLUTIONS AS FAST AS POSSIBLE. WITH SkillPak™ PRE-PACKED COLUMNS, WE PROVIDE A TOOLKIT THAT SUPPORTS FAST PURIFICATION METHOD DEVELOPMENT. HERE WE EXEMPLARILY DESCRIBE THE DEVELOPMENT OF A 2-STEP PURIFICATION WITH SkillPak COLUMNS AIMED TO REDUCE DOWNSTREAM PROCESSING COSTS FOR ANTIBODIES.

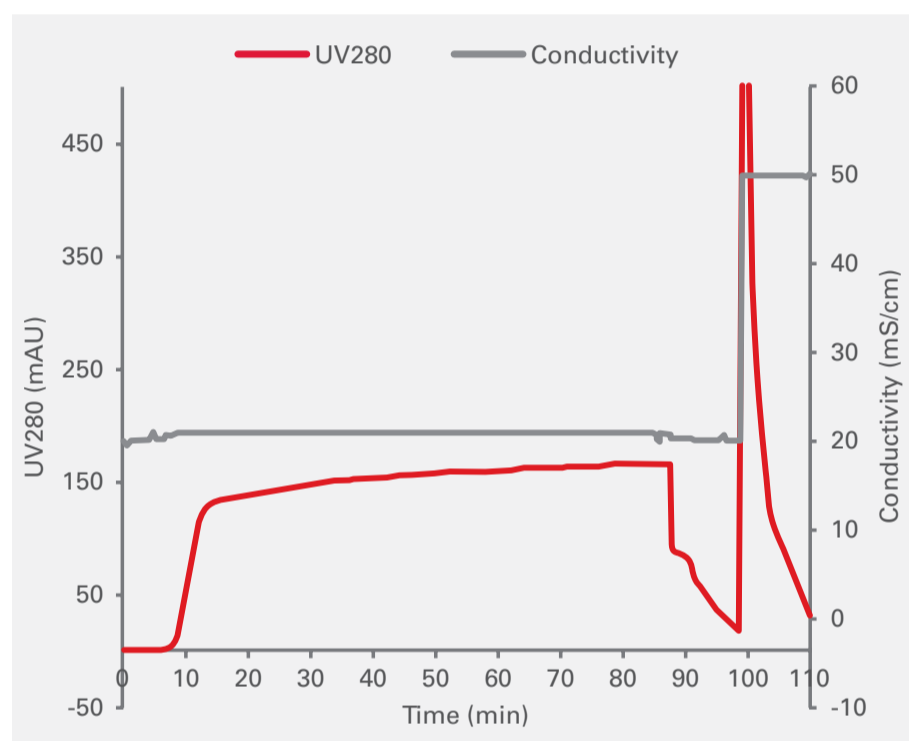
Given the current drive to shorten the development timelines and reduce cost of manufacturing for biological therapeutics, streamlining downstream processing is a necessity for chromatographers and process engineers. This article summarizes a study that demonstrated the benefits of Tosoh's 2-step process for the purification of monoclonal antibodies (mAb) compared to the standard industrial process. Combining high-performance Protein A capturing and a single polishing step on a salt-tolerant anion exchange resin, downstream costs were reduced by 45 % and production output increased by 58 %.

SkillPak 1 mL and 5 mL columns are designed for fast method development or resin screening. They are packed with TOYOPEARL®, TSKgel® or Ca⁺⁺Pure-HA® process chromatography media for bio-separations and can be operated with common low or medium pressure LC systems. The study used a SkillPak 5 mL column packed with TOYOPEARL AF-rProtein A HC-650F in the capture step and a SkillPak 5 mL column packed with TOYOPEARL NH₂-650F anion exchange media in the polishing step.

TOYOPEARL AF-rProtein A HC-650F is a high capacity Protein A resin for the purification of mAbs. It exhibits dynamic binding capacities (DBC) of 70 g/L at 5 minutes of residence time. TOYOPEARL NH₂-750F, a salt-tolerant anion exchange resin, is ideal for the intermediate purification of mAbs and other proteins. Impurities, such as DNA, viruses, host cell proteins, and endotoxins, are removed. Furthermore, because of the relatively low pKa value (between 7 and 9), it also removes mAb-aggregates efficiently. With this unique feature, both polishing steps that are usually necessary to remove all impurities can be combined in one flow-through polishing step.

In previous work, the capturing of the antibody on the TOYOPEARL AF-rProtein A HC-650F was optimized. After the capturing step, a virus inactivation step was introduced by holding the eluate for 1 hour at low pH. The first experiments on the salt-tolerant anion exchanger in bind-and-elute mode proved that the monomer eluted first. Therefore the next step consisted in adapting the method to achieve flow-through purification. For these experiments, conductivities between 20 and 25 mS/cm were used, as the monomer is eluting under these conditions, whereas the aggregates remain bonded to the resin. To achieve the desired purity without a subsequent chromatography step, a conductivity of 20 mS/cm was applied for the platform design (Figure 1).

Both steps were then combined in one integrated process, including the intermediate low pH hold. Protein A has a recovery of 98.8 %, while AEX has a recovery of 91.3 % (20 mS/cm), which results in a total recovery of 90.2 %. DNA, HCP, and leached Protein A were removed to the Limit of Detection of the used assays (see Table 1).



➤ FIGURE 1: FLOW-THROUGH CHROMATOGRAM ON SkillPak TOYOPEARL NH₂-750F

Critical Parameters	Aggregate (%)	Yield (%)	DNA (ng/mL)	Host-Cell Proteins (ppm)	Leached Protein A (ppm)
Feed	0.56		11.0	550	<0.5
Post protein A	1.05	98.8	605	19	5
After AEX	0.00	90.2	<0.2	<30	<0.5

➤ TABLE 1: CRITICAL QUALITY ATTRIBUTES OF TWO-STEP PURIFICATION PLATFORM

The BioSolve (Biopharm Service Ltd., UK) bioprocess analysis software was used to compare the downstream costs of the optimized two-step process with the costs of an industry standard process published by BioPhorum Operations Group. The optimized 2-step process offered 45 % cost reduction per gram compared to the standard industrial process. In addition, process times have been reduced by 58 % due to the elimination of one chromatography step and higher flow rates on the TOYOPEARL resins. The 2-step antibody purification process presented here using SkillPak pre-packed columns combines high recovery with low process costs and processing time. It can easily be scaled up to a pilot plant and eventually to a manufacturing scale for increased productivity and profitability.

-> Check out the full application note bit.ly/2-StepPlatform

07 WHAT'S NEW SEC COLUMNS

SUPERIOR RESOLUTION FOR HIGH ORDER ANTIBODY AGGREGATES

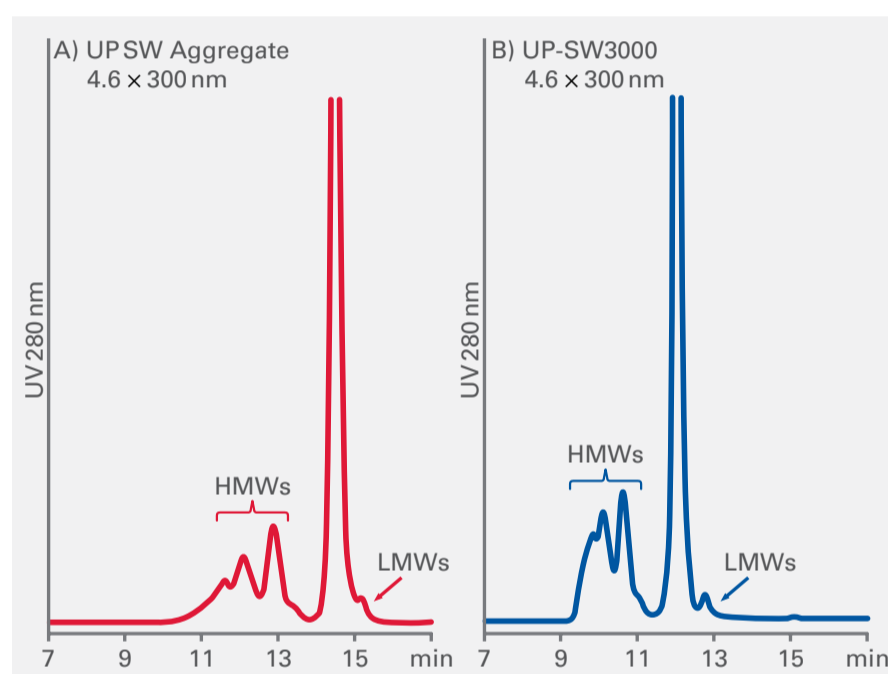
SIZE EXCLUSION CHROMATOGRAPHY (SEC) IS A WIDELY APPLIED TECHNIQUE FOR PROTEIN CHARACTERIZATION AND QUALITY CONTROL. THE MAIN APPLICATION IS THE DETERMINATION OF MONOCLONAL ANTIBODY AGGREGATES. TODAY, NEW ANTIBODY FORMATS ARE ENTERING CLINICAL PHASES, WITH SOME OF THE NEW FORMATS HAVING A HIGHER MOLECULAR WEIGHT THAN CONVENTIONAL ANTIBODIES. TSKgel UP-SW AGGREGATE, THE LATEST ADDITION TO THE UP-SW SERIES OF SEC COLUMNS, IS SPECIFICALLY DESIGNED TO FACILITATE THE ANALYSIS OF VERY LARGE PROTEINS AND HIGHER ORDER ANTIBODY AGGREGATES.

Protein aggregation is a major issue in therapeutic protein development, since the presence of these impurities reduces the potency of the drug formulation, even if non-toxic. Monoclonal antibodies, widely used in the field of biotherapeutics, must be free from these aggregate impurities. In order to fully evaluate the aggregates, a size exclusion column that has a large enough pore size is needed, so that the higher order aggregates are not excluded in the void but separated as a function of hydrodynamic volume.

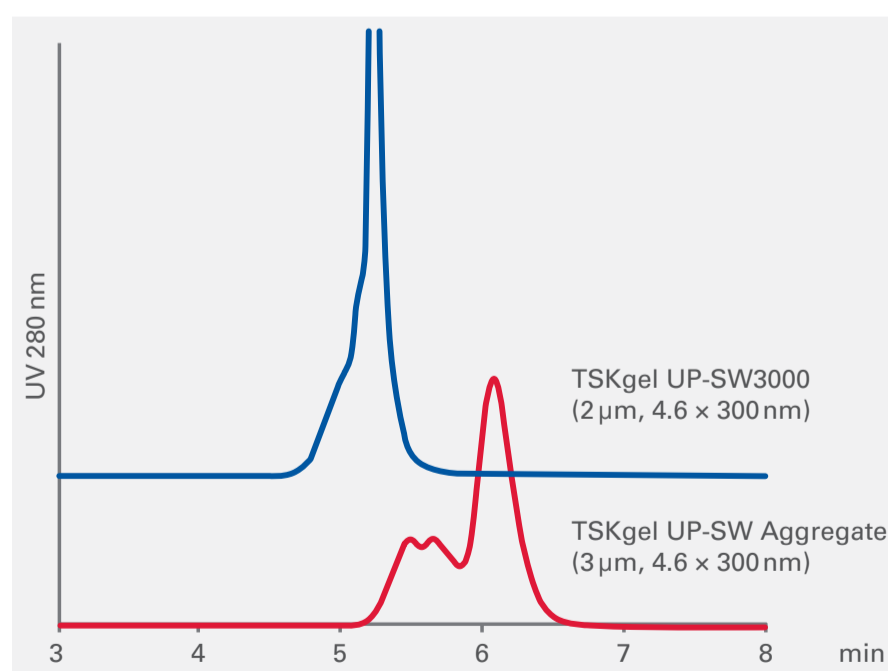
TSKgel UP-SW Aggregate, the latest addition to the UP-SW series of silica-based analytical SEC columns, are 3 μm , 30 nm pore size SEC columns that have been designed with a higher exclusion limit than other TSKgel UP-SW columns. With a separation range of 10-2000 kDa, these columns are ideal for the separation of mAb aggregates, high molecular weight proteins and nucleic acids. Available in 4.6 mm ID x 15 and 30 cm lengths, TSKgel UP-SW Aggregate columns are compatible with both UHPLC and HPLC systems.

The separation of high molecular weight (HMW) and low molecular weight (LMW) impurities of a monoclonal antibody was compared for two columns of the TSKgel UP-SW series, UP-SW3000, a column featuring the same pore size as the renowned TSKgel G3000SW_{XL} SEC column, and UP-SW Aggregate featuring a larger pore size. While the TSKgel UP-SW3000 (B) is ideal to get good separation of both HMW and LMW impurities, the TSKgel UP-SW Aggregate allows a more detailed view on the higher order aggregates (Figure 1).

Figure 2 depicts the analysis of human Immunoglobulin M (IgM) on TSKgel UP-SW3000 and TSKgel UP-SW Aggregate. The molecular weight of IgM is much higher than that of IgG. This is the reason why the larger pore size TSKgel UP-SW Aggregate column is better suited to analyze the HMW impurities of IgM. While TSKgel UP-SW3000 does not resolve monomer and aggregates, TSKgel UP-SW Aggregate allows determination of the aggregate content.



► FIGURE 1: Analysis of mAb Aggregates



► FIGURE 2: Separation of IgM monomer and aggregates (1. Aggregates, 2. Monomer)

08

WHAT'S HAPPENING VIDEOS AND VIRTUAL EVENTS

#CHROMATOGRAPHY EXPERTS@HOME

COVID-19 FORCED ALL OF US TO WORK FROM HOME ON SHORT NOTICE. SO HOW WERE WE SUPPOSED TO RECORD THE PLANNED SERIES OF EDUCATIONAL VIDEOS WITH OUR TECH SUPPORT COLLEAGUES THAT WAS TO BE BROADCASTED FROM OUR LARGE AND MODERN LABORATORIES AT THE EUROPEAN HEADQUARTERS IN GRIESHEIM? OF COURSE THE CHROMATOGRAPHY EXPERTS HAD A SOLUTION!

The popular training workshops that have been held for over twenty years suspended, office and laboratories in Griesheim closed for several weeks for both the public and employees, and all colleagues are working from home. How to create a series of educational videos on chromatography under these circumstances? We found the solution in recording the videos – with limited technical equipment – in our home offices and it turned out to be fun!

Meanwhile the first two issues of our series, named #chromatographyexperts@home, have been completed and are available in our social media channels. The first issue explains the basics of multi angle light scattering (MALS) detection and the second issue is dealing with Fc receptor affinity chromatography that can be used to quickly assess mAb glycoforms.



CHECK BOTH VIDEOS HERE: [HTTPS://WWW.TOSOHBIOSCIENCE.DE/EDUCATIONAL-VIDEOS](https://www.tosohbioscience.de/educational-videos)

NEWS & EVENTS | MEET TOSOH BIOSCIENCE IN THE VIRTUAL WORLD

UPCOMING EVENTS

- MOST LIVE EVENTS IN 2020 ARE CANCELLED OR POSTPONED TO 2021. NEVERTHELESS, SOME EVENTS ARE STILL ANNOUNCED FOR THE SECOND HALF OF 2020 AND YOU CAN FIND THE LATEST UPDATES HERE [WWW.TOSOHBIOSCIENCE.DE/NEWS-EVENTS/EVENTS](https://www.tosohbioscience.de/news-events/events)

IN THE MEANTIME....

- ...MEET OUR CHROMATOGRAPHY EXPERTS FOR INDIVIDUAL CONSULTATIONS IN THE VIRTUAL WORLD. AS PART OF THE SCIENTIFIC COMMUNITY, WE UNDERSTAND THE CHALLENGES YOU MAY FACE AS YOU RETURN TO WORK OR USE THE TIME IN THE HOME OFFICE FOR PLANNING AND DOCUMENTATION. TO SUPPORT YOU AS MUCH AS POSSIBLE, WE OFFER INDIVIDUAL APPOINTMENTS WITH OUR CHROMATOGRAPHY SPECIALIST TO DISCUSS SPECIFIC TOPICS ONE BY ONE.
MAKE AN APPOINTMENT HERE: [HTTPS://WWW.SURVEYMONKEY.DE/R/TOSOH_EXPERTSEMINAR](https://www.surveymonkey.de/r/tosoh_expertseminar)

- IN ADDITION, WE RECOMMEND THE VARIOUS RESOURCES THAT WE PROVIDE ON OUR WEBSITE, OUR SOCIAL MEDIA AND ON OUR YOUTUBE CHANNELS:
[HTTPS://WWW.TOSOHBIOSCIENCE.DE/ABOUT-US/CONTACT/SOCIAL-MEDIA](https://www.tosohbioscience.de/about-us/contact/social-media)