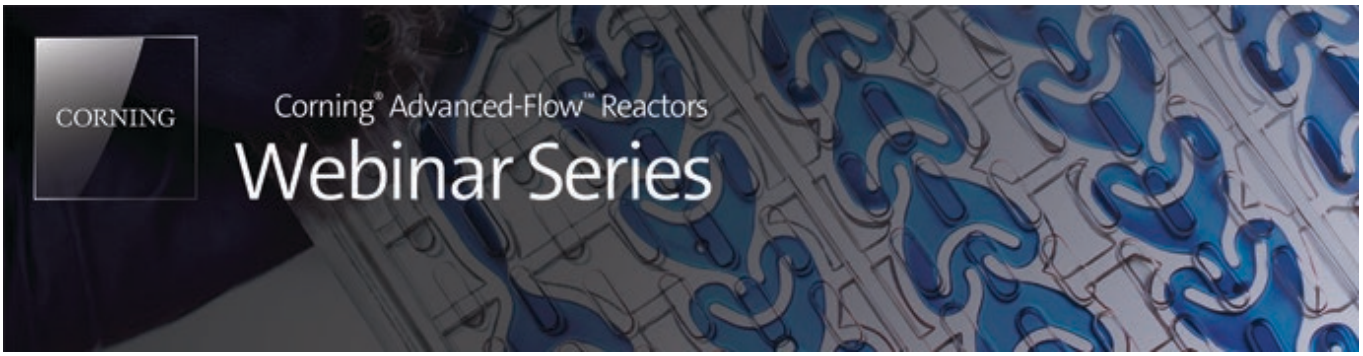

Questions & Answers

Q1: Can you comment about peristaltic pumps?

A: Peristaltic pumps are a type of positive displacement pump. The main advantage of peristaltic pumps is that nothing but the tube touches the fluid.

Because only the inner bore of the tube touches the fluid, they eliminate the risk of the pump contaminating the fluid, or the fluid contaminating the pump. However, the user must ensure that the pump tube materials, including the standard fittings (wetted parts), are compatible with the chemicals being injected. Also, the user must keep track of how many hours the pump has been running (most manufacturers rate tubes lifetime in hours).

Their main disadvantage is the limited pressure range. They are usually limited to maximum discharge pressures of around 8 bar, for the most performant ones. Moreover, when used for micro filling, peristaltic pumps are calibrated to provide no more than approximately 1.3 bar of pressure. Therefore, they are not suitable for Corning reactors that work up to 18 bar.

Older technology peristaltic pumps can present pulsations. Two key design features allow the peristaltic pumps to be accurate for dispensing: the use of multiple rollers and using offset rollers.

Q2: What kind of filter do you recommend in order not to clog the filter/ increase the pressure drop too much?

A: Choosing the correct filter is always a compromise to find between filter volume, size, and surface. It will depend on the type and the environment of use. A filter for a production unit will be different from the filter necessary at lab scale. To give some very general tips, pleated filters are usually a good compromise to achieve a high filtration surface with a small volume. In some cases, it can make sense to have two filters in parallel with the possibility to switch from one to another without interrupting the flow.

This allows you to change/clean the cartridge without interrupting the operations. Another option is to dedicate filters to single lines (one for the starting material, one for the rinsing solvent) in order to minimize the switches of liquid running through the filter.

Q3: How to clean Nitric acid? During washing of reactor, preferring a continuity of solvents with a miscibility rather than heptane and then water after nitic acid…

A: Ideally the cleaning solvent should always be miscible with the liquid to clean and to remove from equipment. The specific case of concentrated nitric acid is a challenging one as, according to compatibility tables, very few liquids can be mixed with nitric acid without the risk of forming hazardous mixtures. The only compatible solvents are alkanes like hexane, heptane or paraffin oil, which are unfortunately not miscible, creating some issues in stagnant zones or dead volumes. Water is miscible but generates a lot of heat when mixed with nitric acid, which can lead in the worst case to the rupture of a pump head. The logic behind using heptane is to push out a maximum of the acid before switching to the miscible solvent, water, that will remove the last traces. A similar approach is to use nitrogen gas to flush the line before using the water. In all cases, care has to be taken in the design and setup of the lines and the choice of materials as with water dilution the nitric acid can become very corrosive at concentrations around 30% to 40%.

Q4: What would you recommend to pump nitric acid based on the materials of check valves?

A: It will depend on the concentration of the nitric acid. Stainless steel 304L and tantalum show the best corrosion resistance among the metals along a wide range of concentrations, so they should be chosen preferably for sensitive parts like check valves. PTFE, PFA and PVDF are also options.

Q5: What precaution should we take while pumping sodium hypo chlorite solution?

A: Hypochlorite solution has two types of issues. First, one has to ensure that the pump is fully compatible material wise. Otherwise, a damage might occur.

The second issue is related to the nature of sodium Hypochlorite solution. As this type of solution (similar to HCl) tends to degas overtime. Therefore, gas might clog and block pumps, especially at lower scale (i.e. Laboratory scale). To avoid this issue, it is better to work with fresh reagents and work under pressure in the system. This will tend to decrease the gas formed.

However, use of these reagents overall requires extra safety.

Q6: The major issue that we face is pumping slurry. How to address this? Is there any promising technology available? How can we ensure the exact amount of solids are being pumped? (stoichiometric amount)

A: Solid handling should be addressed on a case by case basis. Dealing with solids depends on many parameters, including the size of the solid. This is reaction-dependent although the main trend is that these types of reactions may not be the best for flow reactors if solids tend to be big, concentrated or eager to aggregate. The particles should not stick to the reactor wall.

When considering slurry solutions, the pumping system will be the critical point of the installation. This part of the unit will control how homogenous your solution will be for your reaction in the flow reactor. The design of the complete line needs to be adapted, from the choice and potential agitation needed in the storage vessel, to the sizing of the lines to keep a high speed, to the choice and design of the pump head, usually a membrane pump. There is no universal equipment configuration for pumping slurries, but each case will have to be treated specifically.

Q7: For faster settling velocity can we go with gravity flow feeding?

A: No, the pressure necessary to feed our reactors can go up to several bar (maximum 18 barg) so gravity is not enough to feed a flow reactor, but lines with solids should always be built with a slope so that no settled solid can accumulate over time.

Q8: Can you suggest a suitable pump for chlorosulphonic acid in G1 reactor?

A: Chlorosulphonic acid is very reactive towards traces of water, generating HCl and releasing a large amount of heat. Therefore, initial rinsing of the equipment with a dry solvent is recommended to avoid issues and damages in the pumps (uncontrolled environment). In terms of compatibility, metal free dosing lines are recommended for this reagent. Therefore, membrane pumps could be an option. With dangerous reagents, rinsing the systems before and afterwards is recommended. This reagent does not seem to have particular issues in term of viscosity (ca 4 centipoise at Room temperature).

Q9: In your presentation you always indicated the max flow rate of your systems but what about the minimum flow that can be reached for Lab equipment for which you can assure precision of the pumps?

A: The Lab Reactor System contains HPLC pumps. To ensure high accuracy and precision of the pumps, they should be used at minimum 1ml/min. However, this is not generally valid and it is recommended to test the flow rate range in the lab with the fluid that you need.

Q10: What future improvements to the technology in general is of particular interest/on the horizon at the present moment?

A: Corning Advanced-Flow Reactors continually expands our portfolio and expertise to meet market needs. We have an R&D team looking into new capabilities for all reactors and cases. Corning AFR tends to follow the general needs and improvements. Amongst them, topic like automation, in combination with PAT and AI are trending. We encourage people facing an issue/technological gap to contact us and see how we can collaborate on a solution.

Q11: Any suggestion on chemical compatibility choice?

A: The first step in the equipment selection process is to always check a material compatibility chart. Use a strict compatibility chart that takes in account the localized corrosion and not only the general corrosion (as a chart dedicated for Coriolis flowmeters or other sensitive equipment).

Q12: What's the typical pressure drop of the Low-Flow reactor on the heat exchange side? Is there a heater/cooler you recommend to use at lab scale?

A: As the Low-Flow is the only reactor with heat exchange in the series (for standard configuration), pressure drop will be linked to the size of the reactor. But in general, your heat exchanger should have at least 1.2 bar of pump power in order to get right flow.

Q13: Do you have any suggestions on how to operate when a great amount of gas is generated in the process (as a side reaction)?

A: Generating gas represents potentially two issues. First, it potentially involves a dangerous gas which has to be dealt with (flow separation/dilution/extraction). This is performed downstream and has to be addressed during the risk assessment process.

Second, the generation of gas tends to push and flush the liquid out of the reactor too fast, therefore reducing the efficiency of the reaction by decreasing the residence time. The best way to address it is to use a back pressure regulator and limit this effect as much as possible (the gas takes up less space under pressure).

Additionally, attempts at optimizing where the gas formation occurs (preferably closer to the outlet of the reactor) is a potential way to reduce the drawback of such reactions.

Q14: Where to place the pressure relief valve?

A: The place of the pressure relief valve will depend on the equipment that you want to protect. You should connect this valve as direct and close as possible to the equipment being protected. One point to consider is if it should be placed before or after the flow meter which is on the pressure side of the pump. In case it is before the flow meter, in case the PRV opens, the flow meter won't see any flow and the automation would speed up the pump. In case it is after the flow meter it is necessary to check and ensure that the flow meter pressure cannot be damaged by the pressures that could be build up in front of it. These are typical considerations that need to be considered during safety reviews of the system.

Q15: Do we have a standard for suitable viscosity of solvent used in flow system?

A: The limitation will come from the combination of viscosity, duration of the reaction and throughput. As a rule of thumb, we consider that applications with viscosities of 50 to 100 cPo can only be run if the reaction time does not exceed a few 10thof seconds.

Q16: Please let us know the pumps having oleum nitric acid sulfuric acid resistance along with high pressure rating around 200 bar max and viscosity of 10000 cp and must have heating or cooling option.

A: In general, our expertise covers the pumps that can be used with our equipment, thus with pressures up to 18 bar and viscosities of up to 100 or 200 cP.

At 200 bar you can find a metallic pump. As for all the equipment, you need to verify the compatibly of your fluids with the materials in the contact with the liquid.

Q17: Do you know what kind of pumps are compatible with strong bases and with strong acids?

A: The first step in the pump selection process is to check a material compatibility chart. Use a strict compatibility chart that takes in account the localized corrosion and not only the general corrosion (as a chart dedicated for Coriolis flowmeters or other sensitive equipment). Care should be taken as the compatibility with different materials can vary

with concentration and temperature. Also, the fluid velocity can play a role in the corrosion.

For example, for **nitric acid**, high chromium-containing alloys and strong passivating metals like tantalum are the most resistant. The most commonly used material is 304L stainless steel. PTFE is also compatible with nitric acid.

Hydrochloric acid causes severe corrosion due to strong acids combined with chlorine. Tantalum and zirconium are the few materials resistant to hydrochloric acid's corrosive nature. PTFE and PVDF are also compatible with hydrochloric acid.

For **sodium hydroxide**, stainless steel can be used if no chloride is present in the solution. If sodium hydroxide is mixed with water containing chlorine, nickel alloy C22 should be preferred. PTFE, PP, FFKM are also compatible with sodium hydroxide.

Q18: In case of air operated diaphragm pumps, what is the contact parts MOC?

A: An air operated diaphragm pump is a type of positive displacement pump that uses compressed air as a power source. They can be constructed using several materials. Therefore, it is important to determine the compatible materials with your fluid, in order to select the adapted pump best suited for your process. However air operated diaphragm pumps tend to show high pulsations and are limited in the pressure they can generate, so it must be carefully investigated if it is suitable or not.

Q19: Are diaphragm pumps compatible with organic solvents?

A: A diaphragm pump (also known as a Membrane pump) is a positive displacement pump. They are highly reliable because they do not include internal parts that rub against each other and do not have sealing. In general, diaphragm pumps can be made in several materials of construction, compatible with organic solvents. The first step in the pump selection process is to always check a material compatibility chart.

Q20: There seem to be a lot of references on large scale nitration with your reactors. Can you give more details on how to choose the materials of construction of the pump or dosing line specifically for nitric acid ?

A: It will depend on the concentration of the nitric acid. Care should be taken as the compatibility with different materials can vary with concentration and temperature. Also, the fluid velocity can play a role in the corrosion.

Stainless steel 304L and tantalum show the best corrosion resistance among the metals along a wide range of concentrations, so they should be chosen preferably for sensitive

parts like check valves. A metal free solution can also be used using PTFE, PFA or PVDF materials.

Q21: Is it possible to carry out solid or suspension with dosing lines?

A: When considering slurry solutions, the pumping system will be the critical point of the installation. This part of the unit will control how homogenous your solution will be for your reaction in the flow reactor. Slurries are divided into two general categories: non-settling or settling. Non-settling slurries contain very fine particles, which give the illusion of increased apparent viscosity. Settling slurries are formed by coarse particles that tend to form an unstable mixture. The design of the complete line needs to be adapted, from the choice and potential agitation needed in the storage vessel, to the sizing of the lines to keep a high speed, to the choice and design of the pump head, usually a membrane pump. There is no universal equipment configuration for pumping slurries – each case will have to be treated specifically.

Q22: How can you avoid back flow ?

A: Most of the dosing lines we deliver include a check-valve preventing liquid flowing back into the line. Additionally the lines integrate closing valves that can be actioned to protect the line. The reciprocating pump working principle is also relying on check valves included in the pump head, preventing any back flow of the liquid.

Q23: As a non-chemist, can you describe how frequently the fluids should be flushed from the instrument if the instrument is used intermittently?

A: As a general rule, it is good practice to clean and rinse the equipment before and after use. Of course, it is important to make sure the equipment is fully clean after the use of reagents.

If the idle time lasts for a few days, no rinsing and keeping the instrument under a stable liquid can be OK. If in use on a daily basis, it is important to clean it regularly but, in this case, it is possible to leave it under solvent if the gaskets and other more sensitive parts can handle it well (e.g. no swelling). To choose the appropriate solvent for short term storage make sure there can be no fouling, precipitation, scaling or otherwise degradation of the solvent. For long term storage (longer than 1 or 2 weeks) it is recommended to dry the equipment.

Q24: Low viscosity two reactants reacts with each other by generating the product with high viscous product with exothermic reaction. How you will select the pump at feed as well as heat control.

A: In the case an intermediate is formed in situ in an exothermic way, it is good to calculate/estimate beforehand the maximum heat generation to ensure the reactor is capable of dealing with the heat produced. Once the heat generated is known, it is possible to carry out calculation at the heat removal capability of the system.

Practically, to avoid issues with highly viscous intermediates, it is important to initially work in diluted conditions. This will help dealing with both exothermic and viscosity related issues. For more details, do not hesitate to contact us.

Q25: If the same reaction is endothermic and the product is viscous, then what is recommended for feed pump selection?

A: In the case an intermediate species is formed in situ, with a large exotherm and high viscosity, it is important to select pressure which handles high viscosity well as they will have to push the liquid forward. A membrane or piston pump could do. However, it is worth testing the reaction diluted at first. In this case, the extra solvent will accumulate the heat and reduce the viscosity. Checking the temperature and pressure over time is very important.

For the selection of heat control, first calculation of adiabatic maximal heat reached within the system can give a first good approximation of the system capability to handle the heat generated.

…continued on next page…

Q26: For the metering have you seen performance issues at low flow with any particular metering type? Which metering type has been generally most robust?

A: There is no generally valid answer for all the fluids. It will depend on the type of fluid to be pumped, as rheological parameters of the fluid can play an important role on the flow.

All the pumps that were presented in this webinar are for the range starting with 1ml/min. If by low flow rates you refer to microliters, other technologies can be more robust, such as syringe pumps. But remember to consider the material compatibility and the

operational pressure range. If possible it is always recommended to have a flow meter calibrated for the desired flow rate included in the system.

Q27: Is there an option that includes multi-channel peristaltic pumps in order to minimize pressure fluctuations?

A: In general, the pulsation of the peristaltic pumps is reduced by using multiple rollers and using offset rollers. However, we usually don't recommend using peristaltic pumps because of their low pressure range.

Q28: Do diaphragm pumps' diaphragm come in contact with products?

A: Yes it does, the diaphragm will push the liquid into the reactor.

END