Pharma & Biopharma

Requirements profile for WFI pumps

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Requirements profile for WFI pumps

GMP- / FDA-compliant water systems

1. The media

Water is not only the stuff that all life on our planet has developed from. Water also covers 3/4 of our earth's surface and is the most important element for man, animals and nature. The water that occurs in nature is more or less strongly contaminated with germs, depending on it source. Our potable water must be prepared as well to be used as a basis for pharmaceutical solutions, buffers, detergents, solvents in biotechnology and medical technology – e.g. for dialysis, parenteral medicines and infusion solutions. This highly pure water according to DAB 10 (aqua ad injectabilia) or water for injection (WFI) is produced of potable water or purified water. It must be free of pyrogens and sterile with a germ threshold of < 10 KBE/ml. Based on conventional distillation, there are several process steps today that will eventually lead to a quality corresponding to highly pure water. Selection of the materials, line routing and control technology, sterilization and CIP capacity of the components used – such as pipes, fittings and pumps – and the construction features of the plant components are very important for ensuring a pharmaceutical facility's quality.

2. The requirements profile

Pumps for use in highly-pure water facilities (WFI), plant in the pharmaceutical industry, biotechnology and sterile process technology are subject to different laws and higher safety standards around the world. In spite of being simple to operate, they must offer the highest biological safety and must not have any negative influence on sensitive products due to unfavorable hydraulics. In the European area, the "DIN EN 12462 biotechnology" specified performance criteria for pumps, the first specific definitions for cleaning and sterilization capacity, leakage tightness, materials and their surfaces, as well as constructional details regarding the CIP/SIP capacity of pumps. Specifically, the surface roughness of the special steel used in pumps is dealt with here and the electrochemical final treatment is emphasized as an optimal prerequisite for a smooth and low-particle surface. Design details such as the length-to-width ratio of gaps, are defined at < 1.5 and the ratio of length to diameter for dead spaces is indicated at < 2. This standard draft also names the test to be applied to certify the cleanability of plant components for sterile processes. These are largely in compliance with the test method created by EHEDG. Further proof that the basic rules of hygiene-compatible design have been observed and cleanability of the components has been achieved was developed by the specialist department "Sterile process engineering in VDMA" together with the Chair of Apparatus and Plant Design at the TU Munich/Freising Weihenstephan. This test system with the designation "QHD" – Qualified Hygienic Design – is broken down into two test stages. Stage 1 comprises the theoretical proof of hygiene-compatible design and stage 2 is verified by a standard test developed by the chair. This test method is based on the ATP test, with the bioluminescence serving as an indicator for impurities of surfaces.

3. The hygienic design

Main criteria for cleanability of pumps include the cleaning-compatible construction, gap-free design of all inner parts and avoidance of dead spaces under observation of the ratio of length to diameter, which should be between 1 and 2. This applies, among others, to the sealing space of the slide ring packing and the arrangement, application and sizing of the residual emptying by diaphragm valve.

Figure 1: Drain valve

The surface topography of the materials used is also integrated into the criteria for cleanability in terms of the physical properties and possible habitats for germs. The stainless steel centrifugal pumps of the GEA Hilge HYGIA and GEA Hilge CONTRA series meet these requirements in full in terms of cleanability (cleaning-in-place), sterilizability (SIP) and design. This also applies to the materials used and their surface properties, which become the European standard for the area of pharmaceutics and biotechnology according to DIN EN 12462. The CIP-capable and sterilizable shaft seals are freely placed in the product space and have an o-ring seal against the housing cover and the impeller arranged according to hygienic design. This sterile sealing construction is available in single-acting and double-acting tandem arrangement, flushed pressure-free. GEA has developed a special solution for particularly sensitive applications: A double-acting slide ring packing in tandem design that can be operated with an overlaid pressure. This gasket particularly innovatively combines the benefits of "real" back-to-back slide ring packing with the requirements that sterile applications pose in particular to slide ring packing: Cleanability, sterilizability and no dead spaces. The housing gasket is inserted gap-free according to the criteria of sterile technology. All gasket parts and the materials used are FDA-compliant. The stainless steel pumps of the GEA Hilge HYGIA series in the power range of up to 110 m^3/h and delivery heads of up to 70 mFls as well as the GEA Hilge CONTRA series in the power range of up to 40 m^3/h and delivery heads of up to 160 mFls were also tested for their cleaning capacity and accepted according to the provisions of the European Hygienic Equipment Design Group (EHEDG).

This examination was conducted by the internationally renowned research center Weihenstephan of TU Munich. The test result not only confirmed that the pumps can be cleaned without residue by cleaning-in-place, but that, in contrast to the reference tube, no residual contamination could be documented anymore either. This perfectly ensures safety of a sterile process control. In addition to this, GEA also has the right to use the QHD-sign of the specialist department for sterile process engineering in the VDMA. This QHD-sign may be used by companies that implement the basics of hygiene-compatible design and that have employees authorized and trained to the directives of QHD qualification.

4. The GEA Hilge CONTRA series

In addition to the GEA Hilge HYGIA series, the innovative single- and multiple-stage pump series GEA Hilge CONTRA has been developed based on the criteria for Qualified Hygienic Design (QHD). This new pump series is executed according to the corporate philosophy using high-quality Cr-Ni-Mo materials of low-carbon quality 1.4404 or 1.4435 (316L) only. In addition to deep-drawn material for the deflector stages, the impellers, pressure pieces and suction covers use forged materials of the same quality. The impellers and guide vanes of the deflector stages are designed openly. The housings and impellers in the multi-stage pumps are sealed, among others, by an o-ring seal in accordance with the criteria of Hygienic Design, gap-free with defined application pressure and with a metal stop. This ensures absolute cleaning capacity and sterilization in CIP/SIP processes and, as a result, safety for the user and operator of a system with sterile process control.

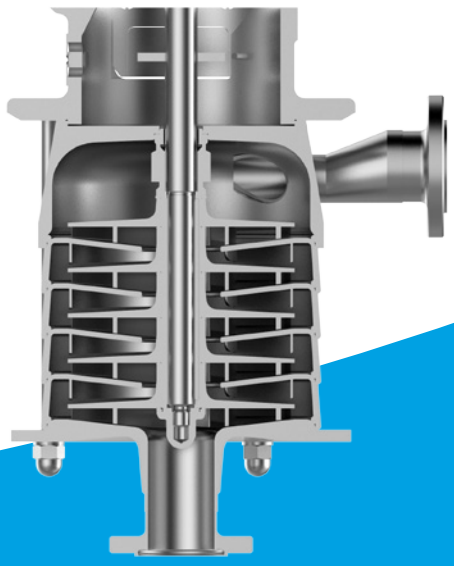

Figure 2: Section of
GEA Hilge CONTRA (5-stage)

In accordance with the high quality standard, the forged impellers have milled contours for optimal efficiency as well as very good NPSH values and smooth running. The entire construction, including the inner sterile mechanical seal (the pump is also available with a double-acting gasket arrangement), exclusively conforms to the criteria of Qualified Hygienic Design (QHD, GMP, FDA) and is also certified to these criteria. Due to this fact and because of use of perfectly pore- and cavity-free materials of Cr-Ni-Mo steel (316L), the pump is outstandingly suitable for use in the pharmaceutical industry, medical technology and in process facilities of biotechnology. Special fields of applications result in the area of highly pure water transport (WFI) and in facilities for production of parenteral medicines and infusion solutions.

The designs

In addition to the classical block design and the pump design on a base plate with load carrier, integration of the GEA Hilge CONTRA series with the Adapta block is of great interest. This Adapta-block connects the pump to any IEC standard motor or Nema motor for the US market without use of a stub shaft, but with an elastic, short serial coupling. This ensures simple maintenance and permits removal of the motor without disassembly of the pump. Subsequent costs are minimized and the wet part of the pump can be left in the system (validation). Another criterion in the area of aseptic processes is the ability of completely draining the pumps. This draining capacity is largely achieved with a diaphragm valve at the bottom-most location of the housing.

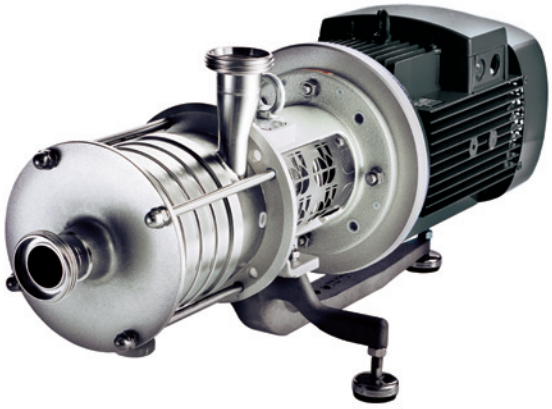

Figure 3: GEA Hilge CONTRA with Adapta bearing carrier

Since this option is not a perfect technical solution in multiple-stage pumps, the GEA Hilge CONTRA is offered in a vertical in perfect condition for this application. The vertical installation guarantees for absolute residual emptying via the suction socket. To ensure residue-free discharge of the liquid from the pump, all product-contacting components have been applied with the corresponding radii and inclinations, including the eccentric pressure piece. The vertical installation additionally saves space within a system, with the Adapta design offering the additional benefit of leaving the entire pump in the system when dismantling or assembling the motor. This is a benefit not only for aseptic processes, in which, however, additional sterilization cycles and validations that may become necessary if the pump is opened or dismantled can be dispensed with.

Figure 4: GEA Hilge CONTRA series in the vertical Adapta design

The materials

In addition to the requirements profile of the design according to hygienic criteria, the selection of materials is particularly decisive for quality and safety in process control in the area of the pharmaceutical industry. Thus, the sterile pumps of the GEA Hilge HYGIA and GEA Hilge CONTRA series use only stainless Cr-Ni-Mo special steels in the low carbon rolled steel quality 316L. The product-contacting surfaces are mechanically ground, polished and electrochemically finished according to the surface standard of the defined sterile class. In particular, the process of electro-polishing is decisive for sterile technology, since a surface that has only been mechanically polished with its sharp

peaks and valleys is predestined for hiding contaminants. In addition to this, the sharp peaks negatively influence the passive layer built up on the special steel that is responsible for the corrosion resistance. It may even be interrupted, which may impair the material resilience against the highly pure water. Electro-polishing levels out such peaks and removes them until a much smoother, more corrosion resistant and low-particle surface results.

Requirements profile for WFI pumps

The sterile pumps of the GEA Hilge HYGIA and GEA Hilge CONTRA series are available in the following surface/sterile standards and materials, with the surface roughness being defined in accordance with ISO 468 and DIN EN 12462 for biotechnology.

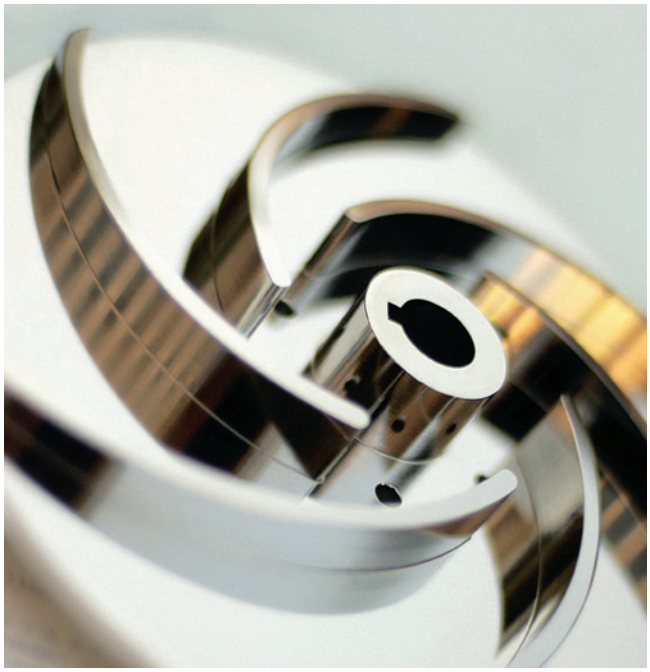

Figure 5: Milled impeller, $R_a \leq 0.4$ µm

DESIGN AND STERILE STANDARD

Surface roughness R_a	Material	Impeller, weldseams
≤ 0.8µm	1.4404/1.4435	Impeller casted
≤ 0.8µm	1.4404/1.4435	Weldseams ground, impeller milled
≤ 0.8µm	1.4435	Weldseams ground, impeller milled
≤ 0.8µm	1.4435 Fe < 1 %	Weldseams ground, impeller milled
≤ 0.4µm	1.4404/1.4435	Weldseams ground, impeller milled
≤ 0.4µm	1.4435	Weldseams ground, impeller milled
≤ 0.4µm	1.4435 Fe < 1 %	Weldseams ground, impeller milled

Ferrite content/"rouge"

Corrosion-resistance of the smooth material surface and influence of the ferrite content play a decisive role due to the high aggressiveness of the highly pure water used in pharmaceutical production. Systems with highly pure water show colorations that range from green to yellow and red and are defined as iron oxide (rust) in analysis. These discolorations and partial deposits are summarized under the term "rouge". Some examinations clearly indicate the possible influence of the δ-ferrite share, which leads to a lower expected corrosion resistance above a 1 % ferrite content in any case. Although Cr-Ni-Mo-steel materials according to the Schaeffler diagram are clearly in the austenitic area, in particular Cr-Ni-Mo cast steel has ferritic sections due to fine phases with high iron and low chrome contents. The occurrence of this δ-ferrite share is due to the process by which the special steel melt freezes, in which ferritic contents occur in addition to the primary austenitic textures. This ferritic content then leads to the development of rust in highly pure water such as WFI that only contains dissolved CO_2 – with all other analysis values below the evidence threshold. The colloidal „rust" (ferritic oxide) may reduce the quality of highly pure water until it drops below the USI quality standards and is rendered useless for pharmaceutics and biotechnology. This "rouge" phenomenon can cover entire sections of tanks, pump and plant components that have a ferrite share in excess of 5 % according to the current scientific insights (among others in the USA) rather than complying with the quality of "low carbon" rolled steel of 316L with defined ferrite contents in WFI systems. There are some welding and processing procedures to supply e.g. pumps in materials such as 1.4435 with a ferrite content of 1 % and to also keep the standardized material AISI 316L (1.4404) at a ferrite content far below 5 % after processing and the corresponding pre-selection. Of course, processing of the materials and aftertreatment as well as final cleaning (passivation) of the system before commissioning are important for the occurrence of "rouge" in addition to selection of the right material. The fight against "rouge" by permanent passivation of entire plant components (a common process today in many companies of the pharmaceutical industry) is effective as well, but constitutes a very expensive solution. Only the consequences of partially unsuitable plant and materials design are targeted here, rather than removing the causes described. It seems urgently advisable to start on a different approach here.

The gaskets

All static and dynamic gaskets have been chosen according to the requirements of their hygienic fitting and design, as well as in light of resilience, CIP and SIP capacities, and to meet the requirements profile of FDA conformity:

- Static gaskets: EPDM with FDA conformity.
  Options: PTFE, FEPS and Kalrez also with FDA conformity
- Dynamic gasket: Single-acting certified sterile slide ring packing
  Option: Double-acting gasket arrangement with internal or external flushing or blocking water supply
  Material pairs: Silicon carbide/silicon carbide, FDA compliant Cr-Ni-Mo steel

The connections

The pumps are designed in such a way that all commercially available sterile connections according to DIN, ASME or ISO and customer-specific versions can be integrated. The following connections are intended by default:

- Sterile thread according to DIN 11864-1
- Sterile flanges according to DIN 11864-2
- Clamp connection according to DIN (e.g. DIN 11864-3), ASME or ISO
- Tri Clover Tri Clamp

Documentation

Documentation is an important part for validation and FDA approval of a pharmaceutical system. GEA supplies the following option for the sterile pumps of the GEA Hilge HYGIA and GEA Hilge CONTRA series as a certified operation purs. to DIN ISO 9001 for the specified standards:

- Test report/acceptance minutes according to DIN EN 10204, 2.2
- Material certificate according to DIN EN 10204, 3.1
- FDA declaration of conformity for the gasket materials and other materials used
- Measuring record surface roughness
- Measuring record ferrite content
- EHEDG test certificate
- QHD certification
- Further inspections and certificates are available on request.

The pump as an integral control component in the WFI system process:

The VE or WFI water system poses different requirements to the pump due to process-related situations. The pump design must consider the maximum acceptance quantities plus minimum flow in the reverse run. The resulting conveying quantity forms the basis for calculation of the power demand of the pump. The conventional centrifugal pump works over-dimensioned across long distances. This is the case particularly for cases like “request of partial volumes” or “only recirculation”, e.g. during weekend operation. This hydraulic partial load operation will emit a larger share of the available energy to the product as heat. This energy form is removed again in part via the coolers – but this solution is process-technically paradox and not economically sensible. It is much more elegant to avoid unnecessary heat input. Using frequency converters between the pump and the supply grid adjusts the speed and therefore the performance of the pump smoothly. Pressure or quantity-dependent control circuits supply any demand with the corresponding pump output. Requests in WFI loops with few demand differences may partially be solved via fixed frequencies (without actual value sensor). The speeds from this are determined empirically, saved in the converter’s memory and then selected digitally. Use of frequency converters permits free definition of the delivery head H and the displacement volume Q of a pump. Running over the common grid frequency clearly improves efficiency of the pump at small volume demands. The cost benefit by use of smaller pumps exceeds the extra costs of a frequency converter. Recent developments in the power electronics sector make it possible to merge the components frequency converter and electric motor. Without any change to the procurement costs for frequency converters, integrated versions are preferable due to the lower connection effort and space requirement (no control cabinet needed).

Figure 6: GEA Hilge HYGIA

The relocation of intelligence from the control cabinet into the field is described in the chapter on “decentralized peripherals”. Field bus systems connect individual subscribers and permit access to functions and data from one control level. The pump with integrated frequency converter is prepared for decentralized use and becomes a transparent actuator in the WFI loop. It determines a comfortable and economically efficient process.

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