

DIALYSIS WATER QUALITY



Why is water quality important in dialysis?



Water is the starting point of any dialysis treatment

For a patient with Chronic Kidney Disease (CKD), good water quality is just as essential to their survival as the dialysis treatment itself.

Water is THE main component of a dialysis treatment. It represents approximately 95% of the total composition of the dialysate.^a

A safe and effective hemodialysis (HD), hemodiafiltration (HDF), or hemofiltration (HF) session can only be performed if the water quality is aligned with national and international guidelines and standards. Drinking water does not meet the minimum requirements defined in guidelines to perform a dialysis treatment.

Therefore, water must go through an additional purification process.

The evolution of hemodialysis treatments requiring higher water quality

Continuous improvements in dialysis products and treatments require higher water quality than before. Here are two such examples.

Dialyzers with high permeability

According to the European Renal Best Practice (ERBP) Guideline 2.1, the use of synthetic high-flux membranes should be considered in order to delay long-term complications of hemodialysis therapy.

High-flux membranes feature a much higher water permeability than other membranes, resulting in the possible backflow of dialysate. **Because water can pass through the semi-permeable high flux membrane into the blood of the patient**, high water quality must be ensured.¹

HDF online

High-volume HDF therapy has been shown to improve the survival of end-stage renal disease (ESRD) patients. According to the ESHOL study, online HDF was associated with a 30% reduction in all-cause mortality compared to conventional high-flux hemodialysis.

In the online HDF technique, **the dialysate fluid, ±95% of which is composed of dialysis water, is directly infused into the blood of the patient.** Hence, the need for the highest possible water quality.

a. Chart based on an acid concentrate 1+44: 1 liter of acid concentrate mixed with 1,4 liters of bicarbonate concentrate 10% and 42,6 liters of purified water in order to obtain 45 liters of ready-to-use dialysis fluid.



Poor water quality puts dialysis patients especially at risk²

Dialysis patient

Weekly water exposure during dialysis 576 L

3 sessions per week, 4 hours per session
Dialysate flow rate: 800 mL/min

External barrier between water and blood:
semi-permeable dialysis membrane

HDF: a percentage of dialysis water is infused directly into the bloodstream of the patient

Renal excretion of toxins and wastes taken up from contaminated water is limited or absent

Additional comorbidities

(e.g. diabetes, hypertension, cardiovascular diseases, etc.) make dialysis patients extra vulnerable to the effects of contaminated water

Healthy individual

Weekly water intake 14 L

Internal barrier between water and blood:
enterocytes of the gastrointestinal tract

Most toxins and wastes taken up from contaminated water are **rapidly excreted renally**

The body of healthy individuals generally copes quite easily with the stress induced by contaminated water

The impact of water quality on hemodialysis patients

Ultrapure dialysis fluid has been shown to have a range of potential clinical benefits – from increased survival rate and better quality of life for patients, to cost savings for healthcare providers.

Use of ultrapure dialysate has been associated with:

1. Reduction in inflammation

The change to ultrapure dialysate lowered the levels of inflammatory markers, including **C-reactive protein (CRP) below 8 mg/Lb³**; CRP levels below 8 mg/L have been associated with a reduced risk of cardiovascular disease and mortality in hemodialysis patients.⁴

Inflammatory markers ³	Number of studies	Number of patients	Baseline value	Mean change	Relative change (%)	P value
C-reactive protein (mg/L)	23	2221	8,63	-3,19	-37%	<0,001
Interleukin-6 (pg/mL)	16	721	25,65	-5,43	-21%	<0,001
Interleukin-1 receptor antagonist (ng/mL)	7	213	0,89	-0,16	-18%	0,002
Tumor necrosis factor-α	8	256	34,58	-13,29	-38%	0,003

2. Reduction in oxidative stress

Oxidative stress is involved in the progression of renal injury, pathogenesis of atherosclerosis, and exacerbation of disease burden in CKD patients.

The **reduction in oxidized LDL cholesterol by 13%³** with the use of ultrapure dialysis fluid is promising. By comparison, a 1-year treatment with the drug atorvastatin has been shown to reduce oxidized-LDL cholesterol by 22,7%, which was associated with a reduction in non-calcified coronary plaque volume⁵. This suggests the beneficial effect of ultrapure dialysate on hemodialysis patients affected by atherosclerosis.

Oxidative stress markers ^b	Number of studies	Number of patients	Baseline value	Mean change	Relative change (%)	P value
Pentosidine (nmol/L)	2	200	1537,79	-263,76	-17%	<0,001
Myeloperoxidase (ng/mL)	2	168	136,85	-66,05	-48%	<0,001
Oxidized LDL cholesterol (U/L)	2	160	51,60	-6,90	-13%	0,024

3. Improvement of the nutritional status

In a meta-analysis of 14 studies, an average **increase of 0,11 g/dL (3%) in serum albumin³** (a surrogate marker of nutritional status) was observed when ultrapure dialysate was used. This increase is especially relevant for dialysis patients, since those with a normal nutritional status only have 0,16 g/dL higher serum albumin levels than patients with a poor nutritional status; a difference of 4,4%.⁶

4. Amelioration of anaemia

When looking at 5 controlled trials using ultrapure dialysis fluid, a significant increase in hemoglobin levels and a reduction in erythropoietin (EPO) administrations per week of 1188 units per patient was observed.^b

The list price of EPO is € 0,0068 per unit In Belgium.⁷ Therefore, this reduction in EPO would translate to a **cost reduction of €8 per week (€452 a year)** per patient in Belgium.



What impacts the quality of water?

Multiple variables impact the water source, its compositions, and its toxicity. Thus, the quality of the incoming water source must be evaluated prior to setting up the water treatment system in the dialysis center, home installation, or in-center unit. The outcome of this analysis will define the configuration and complexity of the water treatment system required for that specific installation.

Contaminants^{2, 8-11}

Based on the water source (e.g. spring, river, etc.), the purification method at the municipal water facility, the transport medium to convey the water from the source to the dialysis center, the location, and so on, the drinking water may contain impurities (e.g. bacteria, endotoxins, minerals, organic and inorganic substances). These contaminants are not inherently toxic in nature, but, if present in high enough concentrations, they can cause adverse health effects.

The most common contaminants are:

1. Inorganic contaminants

Some chemicals are naturally present in the water, some get in the water as a waste product of industrial processes or by leakage from plumbing systems; and others, like fluoride, are added to drinking water for public health benefits:

- Calcium/Magnesium
- Fluoride
- Aluminum
- Chlorine/Chloramines
- Sulfate
- Nitrates

2. Organic contaminants

Substances, such as organics compounds, pesticides, and fertilizers used for agricultural production, pharmaceutical products, and endocrine disruptors can also be found in the some sources of incoming water.

Endotoxins are a major component of the outer cell wall of gram-negative bacteria.

3. Biological contaminants

Microorganisms, such as bacteria, viruses, fungi, etc.

4. Radiological contaminants

Radiological elements could be picked up as water flows through soil or rocks, or due to exposure to industrial waste.

5. Particles

Water may contain suspended particulates, such as colloids, which are responsible for the water's turbidity.

Water sources

Based on the water source, we can anticipate the type of contaminants present in the water:¹²

1. Rainwater

Rainwater collection tanks, such as roof top tanks. The main microbiological contaminants are E. Coli, Enterococci coming from roofing material, and wildlife having access to the roof. However, inorganic contaminates can also be found in these rainwater tanks.

2. Municipal water sourced from surface water

Surface water includes, but is not limited to, lakes, ponds, and rivers. Many organic compounds, microbes and contaminants (e.g. pesticide), and some inorganic contaminants can be found in municipal water.

3. Municipal water sourced from groundwater

Groundwater includes, among others, wells, aquifers, and springs. Its contaminants are generally inorganic compounds (e.g. metals such as aluminum, copper, magnesium) and a few organic materials.

Temperature¹³

Increased inlet water temperature can impact the performance of the reverse osmosis, and henceforth, increase its water production but decrease its quality.





How is high quality water ensured?

National and international standards

Regardless of the origin and quality of the incoming drinking water, the dialysis water must reach a certain quality. Several national and international guidelines specify the minimum standards allowed for water quality in dialysis, such as:

- International Organization for Standardization (ISO)
- European Pharmacopoeia (EPH)
- European Best Practice Guidelines (EBPG)
- Association for the Advancement of Medical Instrumentation (AAMI)
- French national standards

ISO recommendations are the most international and commonly used ones. The most important ISO for water quality in dialysis is ISO 23500 "Preparation and quality management of fluids for hemodialysis and related therapies". It provides users with guidance for handling water and concentrates, as well as the production and quality oversight of dialysis fluid used for hemodialysis.¹⁰

The ISO 23500 series is the base standard for a number of other standards addressing water treatment equipment, water, dialysis water, concentrates, and dialysis fluid.

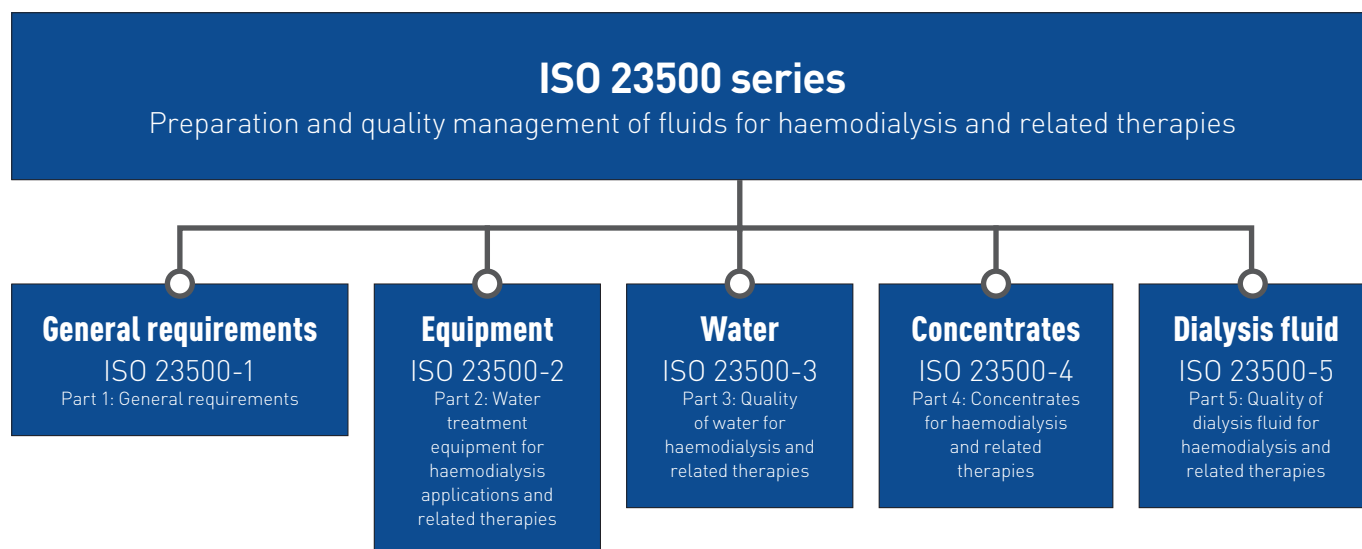
Microbiological ISO recommendations for dialysis water and fluids for HD and HDF:

	Dialysis water ISO 23500-3	Dialysis fluid ISO 23500-5	Ultrapur dialysis fluid ISO 23500-5	Substitution fluid ISO 23500-5
TVC*	<100 CFU**/ml	<100 CFU/ml	<0,1 CFU/ml	Sterile and non-pyrogenic
Endotoxins	<0,25 EU***/ml	<0,5 EU/ml	<0,03 EU/ml	

*TVC = Total Viable Microbial Count

**CFU = Colony-Forming Unit= "measure of bacterial or fungal cell numbers that theoretically arise from a single cell when grown on solid media"¹⁰

***EU = Endotoxin Unit



At present, dialysis water is the minimum quality water allowed for dialysis, but **ultrapure water has become the standard in most dialysis centers**. Ultrapure water has more stringent microbiological criteria than standard dialysis water. It is obtained by having additional ultrafilters that provide a lower bacterial load and endotoxin concentration.

How can water quality standards be achieved and maintained?

In order to ensure high water quality for dialysis, both the proper design and composition of the water treatment system, as well as adequate hygienic measures and maintenance are crucial. Continuous production and distribution of ultrapure water can only be ensured if these four complementary measures are followed:¹¹

Surveillance

The surveillance, or routine monitoring, of bacteria and endotoxin levels is to demonstrate that the disinfection is working properly in order to ensure constant conformance to the maximum limits, as defined by national and international guidelines.

Disinfections

It is a preventive measure to be applied from the moment the water treatment system is in use, not as a corrective measure when bacteria have already proliferated to an unacceptable level. The most commonly used disinfection procedures are heat or chemical disinfections.

Replacement of filters and/or resins¹¹

The timely and periodic replacement of filters and resins, associated with proper disinfection cycles, are mandatory to ensure optimized microbiological results and the long-term production of ultrapure water.

Prevention of biofilm^{11,14,15}

Biofilm is a layer of microorganisms contained in a matrix (i.e. a slime layer). It may contain bacteria, yeast, fungi, and algae. It forms on an inert surface in contact with an aqueous environment that is not disinfected frequently.

Water flux in the water treatment circuit does not completely prevent the adhesion of water-borne bacteria; it only minimizes the formation of biofilm.



Water treatment installations

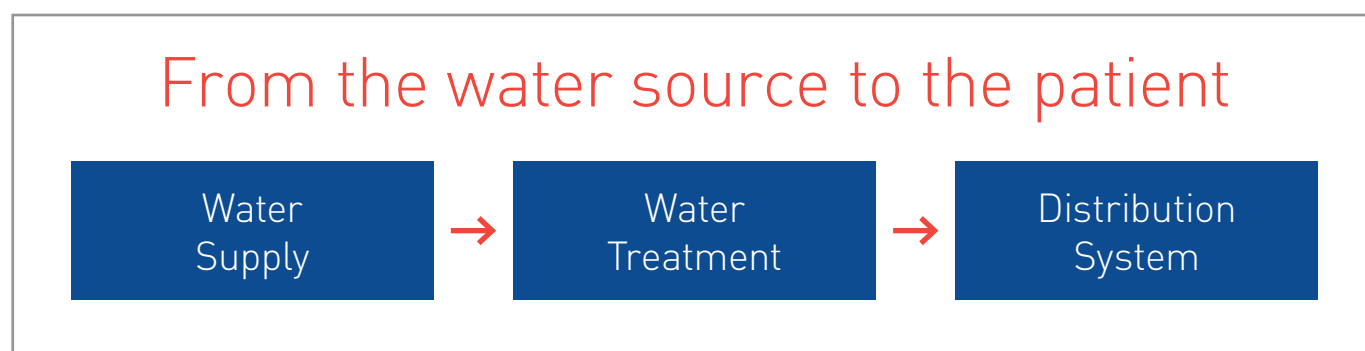


What are the optimal material components of a water treatment installation?

Materials used for the water treatment installation, delivery loop, and storage should also be consciously chosen to ensure that they do not contribute to water contamination or facilitate the growth of microorganisms. The materials should not interact chemically or physically with the type of disinfection chosen.

Material	Installation	No. of fittings	Risk of stagnation	Sodium hypochlorite	Peracetic acid	Heat disinfection
PVC	Medium	High	High	X	X	
SS	Difficult	Medium	Medium		X	X
PEX	Easy	Low	Low	X	X	X
PVDF	Medium	Low	Low	X	X	X
PTFE	Medium	Low	Low	X	X	X

What are the essential parts of a water treatment installation?



The quality of the dialysate delivered to the patient is intrinsically linked to any imperfections in the water treatment chain: from the water supply to the dialysate delivery. Each element of this water treatment chain and delivery system impacts the water quality and can be source of microbial growth or chemical exposure.

In order to provide the best outcome, a good design of a water treatment installation takes into account all of the following:¹⁰

1. Step 1: Water Supply¹¹

The pre-filtration process is required to bring incoming water to a higher water quality that is compatible with the reverse osmosis. This process removes contaminants in order to protect and increase the efficiency of downstream components.¹²

Depending on the incoming water quality, in addition to the ability of the installation to produce and maintain appropriate water quality, Nipro will recommend the following components:

- Inlet water tank
- Turbidex and sediment filters
- Softener
- Activated carbon filter

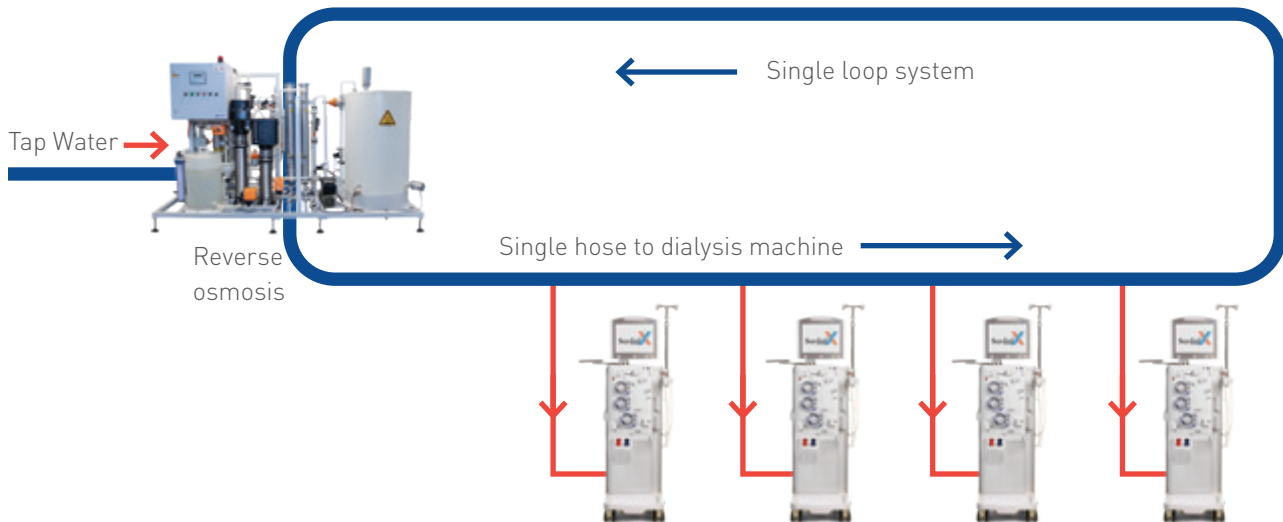
2. Step 2: Water Treatment^{11,16}

Reverse osmosis is a technology used to remove the majority of the remaining contaminants present in the incoming water after the pre-treatment process. Nipro's portfolio includes 4 types of RO Systems, optionally including an ultrafilter or sterile filters, which will remove up to 99% of dissolved salts from the feed water.

3. Step 3: Distribution system

The distribution system or loop is the tubing that feeds permeate to each dialysis machine. Its goal is to provide every machine with a continuous supply of dialysis water.

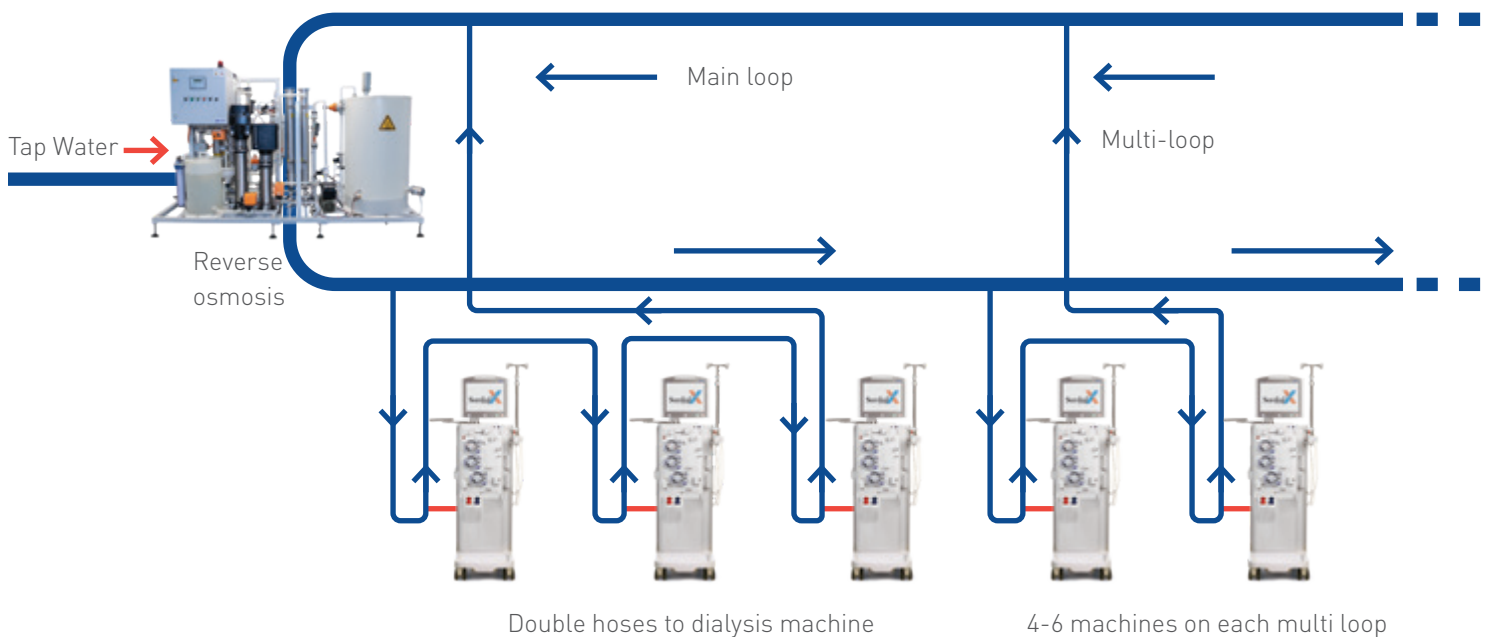
a. Standard single loop system



A standard single loop is generally composed of a main loop, with each machine connected to this main loop by a single inlet hose in which water can remain stagnant if the machine is not running, known as dead space. It can result in biofilm formation, which can trigger acute or chronic reactions in dialysis patients.

b. Dead leg-free multi-loop system

To avoid the dead space between the loop and the dialysis machine, Nipro proposes a multi-loop design connected to dialysis machines while keeping a continuous loop.



What is Nipro's solution?

Nipro Medical Europe takes great pride in providing water treatment systems that fulfill the water quality expectations and regulations that ensure safe dialysis treatments.

Expertise

Active since 2005 | 800+ RO systems installed | Present in 50+ countries worldwide

Manufactured at Nipro Pure Water, Germany

Portfolio

Pre-treatment | Permeate Loop | Concentrate distribution system | Media Supply System

Reverse Osmosis systems



Phoenix One (Single Stage) | Phoenix One DS (Double Stage)

*optional: hot tank for disinfection

* optional: connected solutions



RO Medical



RO Medical Basic

Certified

Full Quality Assurance System | Medical Device Directive | 93/42/EEC Annex II excluding Section 4 |

Quality Management System | ISO 13485: 2016



Pre-treatment

Nipro's Turbidex™, which replaces the multimedia or sand filter, enables filtration at a level below 5 µm, compared to 80 µm for standard multimedia or sand filters. It allows for hyperfiltration efficiency, superior water clarity, and savings on water consumption and costs.



Reverse osmosis (RO)

Phoenix One DS, equipped with a Double Stage RO is designed to provide you high quality water. Waste water from the second stage gets reused in the first stage, reducing the ecological footprint.

The use of high-performance materials, such as PVDF for the piping, significantly reduces the formation of biofilm due to their extremely smooth inner surfaces and water-repelling lotus effect.



Octabin

The new Octabin with top connector contains a large volume of ready-to-use liquid acid concentrate. It is designed to be connected to a concentrate supply system for the delivery directly to dialysis machines, making it environmentally-conscious, space-saving, and nurse-friendly.



Hot Tank

Heat disinfection system for complete sanitization of the permeate loop and all dialysis machines connected. There are no standby costs related, as the tank will fill up only during the heat disinfection. The tank is ventilated with a sterilizing filter to prevent contamination and the filling volume is variable. Automatic disinfection overnight is possible.



Flow Heater +FH

Providing an economic heat disinfection system for the permeate loop. There are no related standby costs.



Phoenix Move

MOVE supplies dead space-free high quality water to each dialysis machine, reducing the risk of biofilm formation while also delivering up to four different concentrates to dialysis machines.

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Nipro Renal Care is a global market leader with over 5 decades providing renal solutions for dialysis and dialysis-related treatment. We specialize in developing dialysis machines, water treatment systems, and a comprehensive portfolio of disposable medical equipment.

In order to address the needs of patients, healthcare professionals, and procurement managers alike, Nipro Renal Care is driven by innovation and patient safety to offer the highest quality products that optimize time, effort, and costs.

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