# Medical Polymers 2004

**15th-16th November 2004, Dublin, Ireland**

## 4th International Conference Focusing on Polymers used in the Medical Industry

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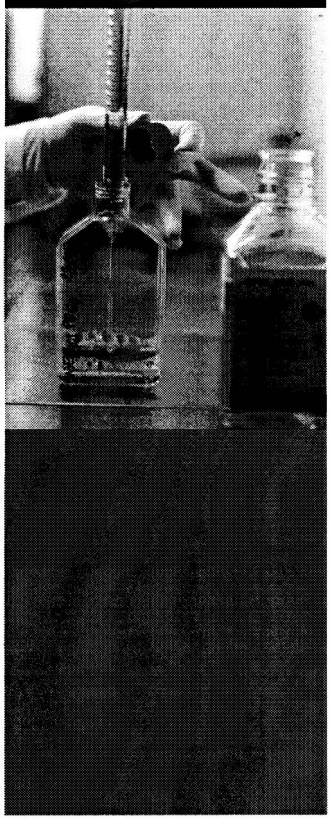

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# MEDICAL POLYMERS 2004

## 4th International Conference focusing on Polymers used in the Medical Industry



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**Rapra Technology Ltd**

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Dublin, Ireland
15-16 November 2004

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# Medical Polymers 2004

15-16 November 2004
Gresham Hotel, Dublin, Ireland

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# MATERIAL SELECTION IN THE DEVELOPMENT PHASE OF HEALTHCARE PRODUCTS

***Dr.Tilo Vaahs,*** *Market Development*
*Ticona GmbH, Professor Staudinger Strasse, D-65451 Kelsterbach, Germany*

## BIOGRAPHICAL NOTE

**Dr Tilo Vaahs** studied chemistry at the University of Karlsruhe and finished with a PhD in Inorganic Chemistry. He joined Hoechst AG in 1986 as Project Leader. After various managerial positions he moved to Ticona in 1997. Currently he is Manager for Industries in Market Development.

## ABSTRACT

After data about the reasons why new general products failed in the market place there will be information why the selection of material is even more critical for new products in the medical area. There is a first toxicological assessment of the polymer based on FDA and EU regulations using the food contact approvals. Then the sterilisation (hot steam, hot air, ETO, gamma, electron beam, x-ray) and the effect on the polymer is discussed. Different categorisation of the final product in terms of the intensity of body contact will be shown and its direct influence on the thermoplastic, which is in the perspective of use for the final product. If direct drug contact is the case for the new product then a whole range of tests for leachable and extractable substances and their effect on the drug itself have to be performed.

---

### 1. Development Start

A look at the reasons, why new products fail in the market place, reveals various reasons.

| | |
|---|---|
| • inadequate market analyses | 29% |
| • product problems / defects | 24% |
| • no effective marketing | 14% |
| • higher costs than expected | 10% |
| • competitive reaction | 9% |
| • poor timing of introduction | 8% |
| • technical / production problems | 6% |

Source: G.Brue: Design for SixSigma (McGraw-Hill)

At least the topics product defects, higher costs and technical problems could be linked to problems with the selected materials for the final product. This material selection is even more critical for medical devices, because in addition to the mechanical property profiles one needs to understand the impact of the polymer on the performance of the final product during application lifetime in terms of

- Toxicological Assessment
- Multi Use
- Single Use
- Sterilisation
- Degree of Body Contact
- Extractables
- Drug Contact
- etc.

Of course the focus here is to ensure patient safety in the end.

Therefore it is a must to involve the resin supplier during the material selection phase to cut out negative surprises in later development phases.

## 2. Assessments

### Toxicological Assessment

A good start is to look at the food contact approvals of the selected polymer grades. All the resin producers and the additive industry have done intensive work and performed toxicity studies to demonstrate the safety of use in contact with food. There are two main regulations:

Code of Federal Registration (CFR) in USA
- each polymer with one paragraph
- description of monomers to be used, the polymer itself
- description of extraction studies
- definition of global migration limits

EC directive 90/128 and following for EU
- summed up as EC 2002/72
- to be translated into national law
- description of polymers
- positive list for additives
- definition of specific migration limits

This means for such a resin used in a medical device, that there is no general toxicity risk for the patient.

### Multi Use vs. Single Use

All the sterilisation techniques are potentially hurting the polymer in a way that the polymer chains are cut. This leads to a reduction of toughness and the polymer parts may break at less load compared to the performance prior to sterilisation. Therefore it is necessary to understand the kind and number of sterilisation processes the medical device has to pass and select the resin accordingly.

ETO sterilisation:
- highly reactive substance to destroy microorganisms
- toxic, carcinogenic, teratogenic chemical substance
- applied at room temperature
- migrates into the polymer
- ABS, PC, PS show high affinity to ETO
- PVC frees not reacted ETO very fast
- Silicones give change of colour due to reaction products
- toxicological assessment of reaction products?!

Radiation:
- radiation leads to energy uptake resulting in split of molecules and generation of free radicals
- death of cells
- radiated product does not emit radiation
- can be used immediately after radiation process was stopped
- applied at room temperature

Gamma Radiation
- high penetration rate
- full pallets possible
- takes several hours

Electron Beam (beta radiation)
- lower penetration rate
- full pallets not possible
- needs less than 1 minute

X-Rays
- high penetration rate
- full pallets possible
- radiation time depends on part thickness

**Degree of Body Contact**

Medical Devices are categorised according to the degree of contact to the human body. In general there are three categories:

- surface devices
  skin, mucosal membrane, breached or compromised surfaces
- externally communicating devices
  indirect blood path, tissue and bone communicating, circulating blood
- implant devices
  tissue, bone, blood

All of these categories are further broken down to the duration of the contact with the human body, which is limited (less than 24 hours), prolonged (24 hours to 30 days), and permanent (more than 30 days).

To each of these cases a recommended set of biocompatibility tests is assigned (ISO 10993-1). For example a medical device, which has only skin contact of less than 24 hours (f.i. the sensor head of an ultra sonic device), therefore needs to pass cytotoxicity, sensitisation, and irritation tests. To avoid any complications in the final approval test of the ready to market device it is very helpful to have the material tested according to the needed biocompatibilities already at the material selection step. This takes out risk of failing in the last device approval step.

**Drug Contact**

As soon as drug contact is involved the legislation for pharmaceuticals takes the lead. Clinical tests are involved and development costs are dramatically higher compared to standard medical devices.
The resins in contact with the drug needs to be assessed for their extractable substances and their interaction with the drug itself. This is specific for each drug based on its chemical nature. Therefore no general approval scheme exists. It has to be tested by the applying pharmaceutical company.

Drug stability tests
- lead to material specification
- require consistent formulation over time (supply assurance)
- guarantees drug performance
- avoids additional specification cost

**3. Conclusion**

For the development of a successful medical device in the market place it is crucial to work closely together with the material supplier in the material selection phase to avoid surprises in later development stages. Food contact approvals and biocompatibility tests are the basis for toxicological assessments, whereas studies of the material performance after sterilisation gives assurance for the lifetime of the medical device.

# DEDICATED POLYOLEFINS FOR THE HEALTHCARE INDUSTRY

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## BIOGRAPHICAL NOTE

**Dirk Matthijs** is working for Borealis as an application development manager for healthcare applications made by moulding.

He obtained a degree of industrial engineer in 1975 at the technical high school of St.Lieven in Gent ( Belgium).

During his whole professional career, which started in 1976, he has been working with plastics. Up till 1989 he was working as a production manager for laboratory disposables made by injection moulding.

In 1989 he started as a technical service engineer for Neste Chemicals – the Neste polyolefin business was later merged into Borealis. Up till 2002 he has been doing technical service in different countries in Europe hence has always done the service for the healthcare applications.

Since 2002 he focused mainly on the development of new polyolefin's for the healthcare, pharmaceutical & diagnostic market

## ABSTRACT

The consumption of polyolefin's is globally exceeding 70 million ton's resulting in an industry which is highly concentrated on volume.

The healthcare-market for polyolefin's is one of the smallest market area's for polyolefin's putting demanding requirements on the materials.

Combining the requirements for both industries can only be done by dedicated materials which comply to the requirements of the healthcare industry.

Special demands like radiation resistance, high transparency, very high stiffness, ....can only be obtained by using special techniques & additives. This presentation will give you an update on the novelties in polyolefin's for the healthcare industry.

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As so many industries, also the polyolefin-producers have undergone drastic restructuring in order to improve their profitability. By the many mergers the number of producers has been reduced drastically. To improve further the competitiveness, the old plants, with a limited capacity, have been replaced by plants with a much higher capacity. As a consequence, the flexibility of producing many references has drastically reduced because too many changes can not be combined with a high quality material.

Due to this whole restructuring, polyolefin producers have less material references available, which makes it necessary to decide which markets will be served. This is strategically important and will mainly depend on the actual materials & the technical capabilities.

Looking to the total consumption of polymers & specific polyolefin's, the amount of polymers used by the healthcare industry is rather limited. Today we see that +/- 50 % of the materials used in healthcare

applications are polymers which leaves still huge opportunities & challenges for the polymer producers. The healthcare industry is a much diversified market with quite strict requirement in each application, leading to a big number of materials which are needed and which are actually used. Of course the quality requirements in the healthcare industry need to be strict followed however keeping the material available for a long period is as well very essential. Development of medical devices or pharmaceutical products can take many years; therefore materials used in this application need to be kept available to avoid delay in commercial launch & re-execution of expensive and time-consuming compatibility tests.

The healthcare-industry is growing not only due to the ageing populations but as well the higher awareness, the anti-ageing trend and the increasing anti-allergic diseases are some of he main causes. At least all West-European countries see each year an increase in the expenditure of the social security.

When considering polyolefin's as bulk materials we could ask ourselves if they are the right polymers for a high demanding healthcare industry. We indeed believe that polyolefin's can bring added value to the whole value chain because they offer a very interesting cost/performance ratio due to several of the characteristics, it's low density and the competitive overall cost of polyolefin's. Being environmental friendly offers to polyolefin applications an extra value, especially in healthcare as most of the waste is incinerated because of the contamination risk.

Borealis is offering since many years polyolefin's to the healthcare market & we will continue doing this. Healthcare is for us an application where we want to invest & grow. Therefore we have created a range of dedicated materials & branded them under Bormed™ to differentiate them from our normal existing product range. This makes them easy to recognize by our customers however as well by everyone in Borealis. Strict SOP's & QC together with well defined logistics are necessary to assure the needs of the healthcare market.

Polypropylene was growing fast in the last decade & is today still one of the polymers with the highest growth. Growth was made possible because it's strong market related development which brought new possibilities in applications. In polyethylene, which is more mature, several novelties were introduced. Of course these new development were initially not created for the healthcare market however we believe it is now the time to consider them when a new healthcare development is made as they are bringing value for money and have proven their effectiveness in other applications.

- **BNT: A PP- nucleation technology for healthcare**

Nucleation gives polypropylene no additional features however brings the properties of polypropylene to a higher level: transparency, stiffness, vicat softening temperature, HDT & hardness are increased. The increased crystallization temperature & speed give potential for faster cycle-time. The change in morphology is caused by additional chemicals added during the extrusion together with the other additives, initiating the formation of crystals. These nucleation agents as talc, sodium benzoate, sorbitols,.. have some drawback in healthcare applications because only a few do appear on the positive list of the European pharmacopoeia & some of them cause too high absorbance on the polymer-extractions.

BNT, Borealis Nucleation Technology, is a propriety nucleation technology of Borealis. The catalyst-system gives the produced polypropylene one of the most effective nucleation which is actually available. As BNT-technology delivers polypropylene with a very effective nucleation it creates the increased properties but as well a potential up till 15 % cycle-time reduction.

Polypropylene produced with BNT is in full compliance with all regulations including the European pharmacopoeia.

BNT-polypropylene does not deliver products with a perfect transparency however their increased HDT & vicat softening point makes them extremely suited for product which need a post steam sterilization. We believe as well that BNT-materials can replace other polymers like hard PVC or PS as they approach their stiffness.

- **Radiation resistant PP**

Sterilisation by radiation is still increasing & replacing other sterilization methods. It is known that polypropylene is sensitive to radiation and it will degrade & become yellow. As during radiation radicals are formed and the solid system gives them very little mobility, long term testing at eventually elevated

temperatures is needed. The transparency of glass is still a reference in the healthcare industry; therefore the combination of transparency and radiation resistance is an ideal combination.

During these long term testing, yellowing & brittleness are the main parameters which need to be monitored. Several times the test was executed on our materials and as a conclusion we can state that 9 weeks of accelerated ageing at 80 °C will give you a very good picture of the material resistance. As in medical devices & pharmaceutical packaging a shelf-life of 5 years is very common, we do advice to monitor during 25 weeks at 80 °C.

Producing a polypropylene which has a good transparency and resist radiation can only be made by using a selected polymer and selected additives; unfortunately the used additives are not yet in the positive list of the pharmacopoeia.

The use of transparent radiation resistant PP was initially driven by the syringes. Today we see an increase in diagnostics because sterile packaging together with optical reading, requiring a high & constant transparency, opens new possibilities.

- **Borstar™ : a new polymerization-technology**

Borstar™ is a propriety technology of Borealis to produce polypropylene & polyethylene. The polymerization is carried out under super critical conditions to enhance the properties of the produced materials by controlling molecular weight & molecular weight distribution.

High density polyethylene (HDPE) is mainly used for bottles & closures to pack pharmaceuticals, diagnostics & fine chemicals. Assuring a high quality and being very competitive are the key-drivers.

The environmental stress-cracking resistance (ESCR) of HDPE is in many cases a drawback & can only be controlled by reducing the density and a higher molecular weight. When the density is decreased the bottle will get less stiffness resulting in a lower top-load of the bottle with increased logistic cost as a consequence. A material with a higher molecular weight (lower MFR) will result in a more expensive processing.

With Borstar™-HDPE it is possible to produce bottles with a higher top-load (higher density) with an improved ESCR and an excellent processing. The same technology can produce materials for injection moulding exhibiting high ESCR with improved processing.

Borstar™-HDPE is not only assuring the quality of the application; with it's excellent processing it is possible to down gauge the wall thickness resulting in a lighter product.
Borstar™-HDPE delivers more for less.

New technologies have created new possibilities in polyolefin's. This has been proven in other market segments and we in Borealis believe that by making the necessary adaptation for the healthcare industry they can bring value either in quality, in competitiveness or new possibilities.

In moulding applications, Borealis is supporting & advising to use the dedicated materials for healthcare applications.

# ADVANCES IN HIGH-PERFORMANCE PLASTICS FOR MEDICAL DEVICES

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## BIOGRAPHICAL NOTE

**Jean-Baptiste Bonnadier** is a Market Development Manager for the European Medical Sector at Solvay Advanced Polymers in London, UK.

His background is Chemical Process Engineering with a degree obtained from Ecole Généraliste d'Ingénieurs (Marseille, France). He also holds a Master in Business Administration for Institut d'Administration des Entreprises (aix en Provence, France).

Mr Bonnadier has been active in the high performance polymers field for 7 years. He was employed at BP Amoco Chemicals in 1997. He worked first in Geneva then in London as Product Manager before moving on to a sales assignment as UK and Ireland Sales Manager in 2001 for Solvay Advanced Polymers.

Since July 2004, he's focussing on raising the awareness on the benefits of high performance polymers for medical devices.

## ABSTRACT

Historically, metals like stainless steel, aluminium and various alloys were the only commercially available materials for demanding medical applications.

Today, despite increasing understanding and acceptance of plastics by the industry, there is still enormous potential for the replacement of metals by polymers as they can provide various functional improvements at lower cost while still meeting the biocompatibility requirements.

Advances in high-performance plastics also mean that resins can withstand rough handling, multiple cleaning, disinfection and sterilisation cycles of all sorts without significant loss of properties, opening up new opportunities in single-use as well as multi-use and reusable devices.

Extensive data supporting this, as well as commercial applications will be shown during this presentation.

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    - Stringent Multi-Use and Single-Use Devices
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    - Conclusion
- Question and Answer Session

## Introduction to Solvay

Solvay has a very long tradition of scientific invention and innovation. The commercial introduction and use of the soda ash process was at the foundation of Solvay in 1863. Today, Solvay has diversified significantly from its original business with over 400 sites and 50 companies around the world and is a widely broad-based chemical and pharmaceutical company.

The annual revenues for Solvay are about 8 billion Euros. It is a publicly traded Belgium company with about 30,000 employees. The main assets of Solvay Corporation can be classified into four business groups (Figure 1) with the Pharmaceuticals, Chemicals and Plastics Businesses representing each about thirty percent of Solvay overall business. The last Business Unit is Plastics Processing and involves about 10 percent of sales of the company.

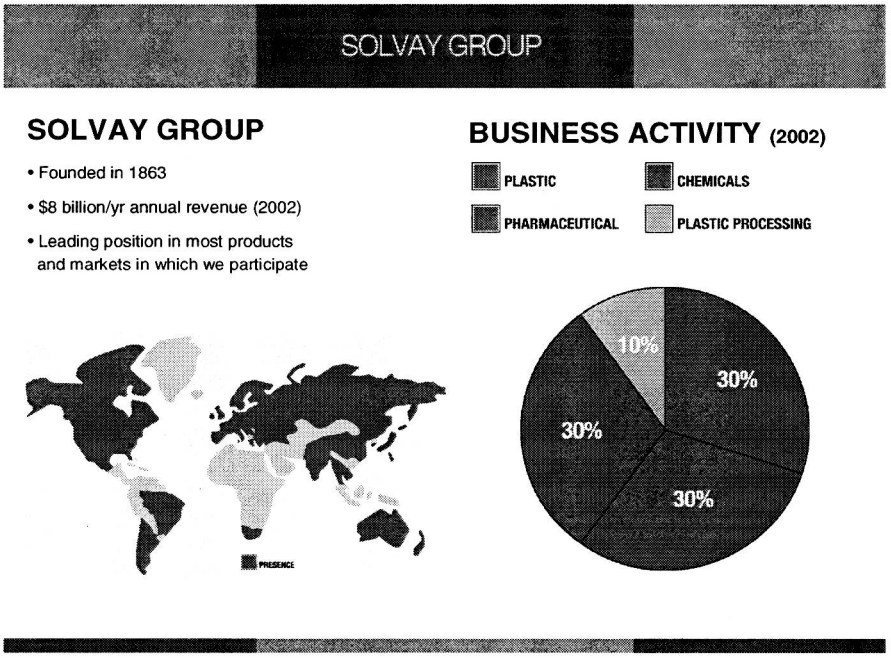


Figure 1

Solvay Advanced Polymers, the engineering plastics business, part of the Plastics Group, was created after the acquisition of the BP Amoco Engineering Polymers business in 2001. The result is a broad portfolio of products (Figure 2) serving various markets, including medical, in America, Europe and Asia.

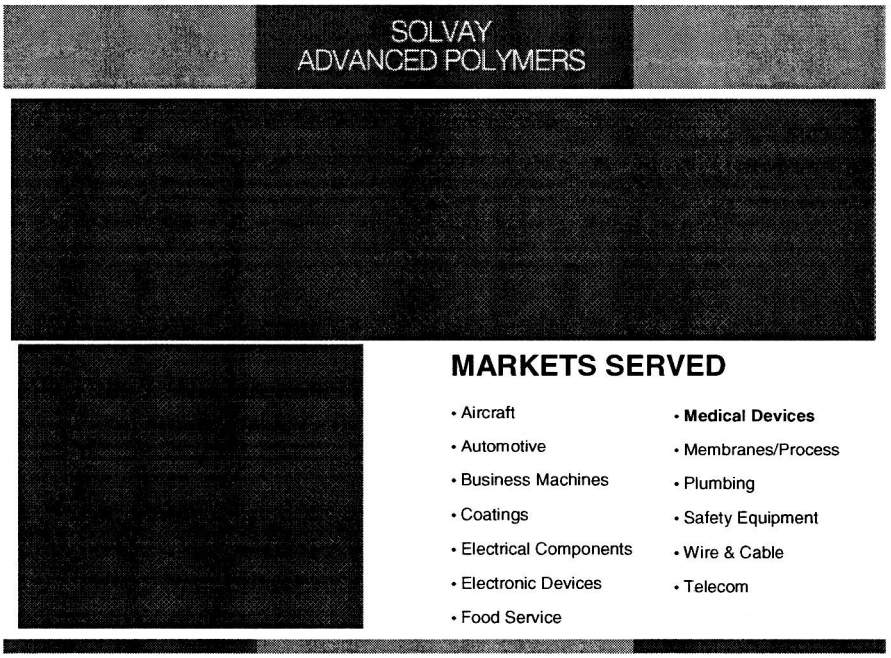


Figure 2

One of the ways of depicting the plastics industry is to show the various types of plastics, either amorphous or semi-crystalline, in ascending level of performance (Figure 3)

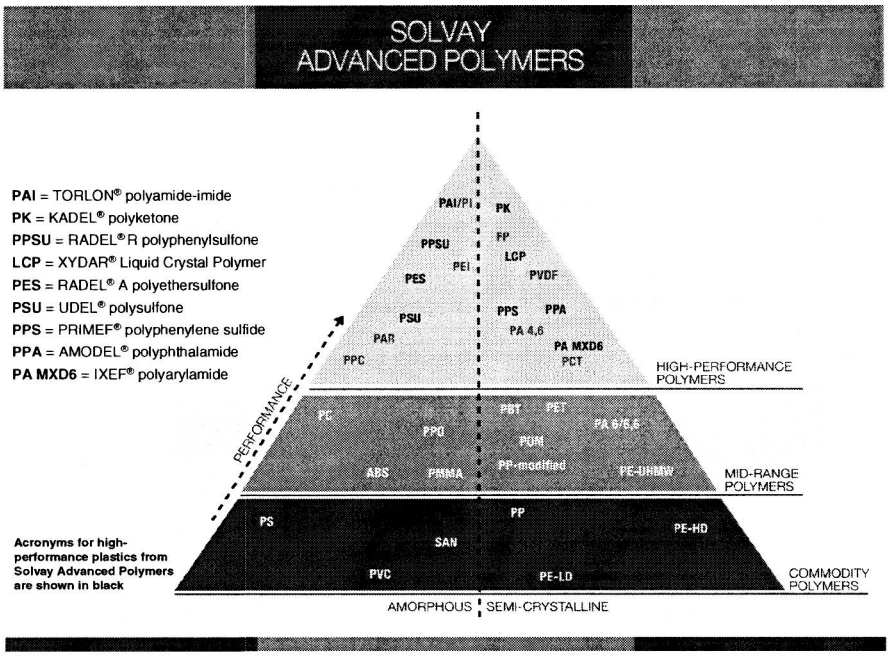


Figure 3

The bottom part of the pyramid has products like HDPE and PP which are very high volume, used commercially for decades and made by 50 to 60 companies in the world.

The next level up is what is called the mid range engineering plastics (PC, ABS, etc...). These are materials that are produced and consumed more in the 1 billion ton range every year and are made by 4 to 5 companies around the world.

The top part of the pyramid relates to the highest performing materials. These are usually not a substitute for other polymers, but a substitute for metal, glass and ceramics. Performance in this case comes in many forms, the most typical being stability at elevated temperature. This performance characteristic would often come in the form of chemical resistance, dimensional stability and mechanical properties at elevated temperature.

Solvay Advanced Polymers' participation is entirely in the high performance segment depicted at the top of the pyramid (products' acronyms shown in bold).

This presentation focuses exclusively on polyphenylsulfone PPSU, polysulfone PSU and polyarylamide PA MXD6 and compare their fitness for use in the medical segment versus metals but also other polymers like polyetheretherketone PEEK, polyetherimide PEI, polycarbonate PC and high heat polycarbonate (e.g. polyphtalate carbonate PPC).

**Advantages of Plastics over Metals**

Historically, metals were the only available materials that could withstand:

-multiple steam sterilization
-exposure to aggressive soaking, cleaning and disinfecting agents
-rough handling