IHK Industrie- und Handelskammer Schwarzwald-Baar-Heuberg

MedicalMountains

Medical device manufacturers look to self-regulation rather than over-legislation from Brussels

Continuation of position paper 07.03.2013

Contents

Introduction

Medical technology manufacturers in Baden-Württemberg are fully aware of their responsibilities to patients, society and their businesses, in line with a long tradition of small and medium-sized businesses which stand out for the quality of their products and commercial integrity. These producers guarantee top quality with their own names.

What has made businesses in the region successful throughout the world is that they know how to create new products responsibly whilst at the same time retaining what is established. This combination of tradition and innovation does not lead to the desired results for patients and users through over-zealous legislation, but only through statutory constraints which businesses can follow and verify.

This led the medical technology initiative Medical Mountains to publish a position paper[1] in March 2013 commenting in detail on the Commission's draft of the new EU medical products law.. This paper was signed by more than 350 competing companies and presented to those in charge in Brussels and Berlin, and was widely welcomed.

These companies and their competitors have joined forces in the cluster organisation Medical Mountains on many points to support the establishment of a consistent pan-European regulation.

What the medical technology companies want above all is a reliable and comprehensive patient care and the best possible protection for patients.

In the wake of the 900 amendment applications in the European Parliament and the political debate which has been taking place since the first draft of the law was published, we find ourselves obliged to use this continuation of our initial position paper to go into two essential aspects of the new regulation in detail once more:

1. **Inflationary upgrading of established medical products into higher risk categories**
2. The demand for more and more **clinical studies**.

[1] MedicalMountains MDR position paper 07.03.2013

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Inflationary upgrading of medical products into higher risk categories

Medical technology devices are safe: they are not made safer by putting them into a higher risk category en masse, like requested in many contributions. We cannot expect upgrading risk categories to have any impact on the criminal activities of a few manufacturers.

Many medical products are already put in higher risk categories in Europe than in comparable international regulated markets today. Since EC Directive 93/42 EEC (2007/47 EEC) was last revised, with the increased testing of class IIa and IIb medical products by notified bodies this involves, it is now easier for medical product manufacturers to get their products licensed in the USA. There are no signs of products being 'upgraded' to higher risk categories in markets like the USA, Canada, Brazil or Japan, even though these use a risk classification system which is comparable with European regulations.

The Medical Service of the Health Insurance Funds (MDK) published a detailed study on approving treatment errors (12,483) in 2012. This showed that medical technology accounted for 0.5%[2] on average of the 3,932 treatment errors recognised as legitimate, the lowest factor compared with treatment management, therapeutic intervention, diagnosis etc.

If we take patient safety seriously, therefore, it is not just design and production we need to look at, but also at how clinical users use and handle products. Improving the organisation and monitoring of medical technology in clinics and practices can improve patient safety at little expense. The medical technology industry expects everyone involved to be more proportionate and more aware of the actual risks involved in dealing with medical technology.

The points still under discussion are as follows:

Rule 6 – first bullet point

Medical devices for cardiac surgery and cardiology: this may possibly be merely a case of omitting the word 'specifically'[3] by accident, but it has disproportionate consequences for many simple instruments, which are upgraded to Class III as a result.

How the medical technology industry sees this, and what its proposed solution is:

› Insert the word 'specifically', retaining the existing established regulation

For more details of this aspect see Annexe I

[2] Treatment error assessment of the MDK community, annual statistics for 2012, published by MDS – Medizinischer Dienst des Spitzenverbandes Bund der Krankenkassen e.V. May 2013

[3] The analogous rule 7 governs it using the word specifically as before

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Rule 6 – second bullet point

Certain circles in Brussels believe thousands of *handheld surgical instruments* should be upgraded from Class I to Class IIa, which is what would happen if Rule 6 second bullet point were omitted as intended. If reusable surgical instruments are seen as an aid to assist the surgeon for simple tissue manipulation, such as holding, clamping, cutting, retracting etc.), upgrading them to class IIa is neither justified nor appropriate.

If reusable surgical instruments are upgraded to risk category IIa, they will come under the supervision of the notified bodies. We estimate the additional administrative costs for companies in the Tuttlingen area alone would be around EUR 95-100 m over a three-year period.

The medical technology industry's assessment and proposed solution:

› Retain the existing grading, as upgrading does not increase patient safety.

› Single-use surgical instruments which do the same job as their equivalent reusable counterparts should be put in Class I 'sterile' (Is).

For more details of this aspect see Annexe I

Rule 6 – third bullet point/rule 7 – second bullet point

Direct contact with the central nervous system (or even the central circulatory system, as many people are demanding) is not sufficient reason to put medical products in class III. We propose a wording analogous with the wording for cardiac surgery[4].

The medical technology industry's assessment and proposed solution:

› Exclude simple instruments as per the wording proposed above.

For more details of this aspect see Annexe I

[4] Analogous with rule 6 – first bullet point, also: **are intended specifically to control, diagnose, monitor or correct a defect of the central nervous system through direct contact with these parts of the body, in which case they are in class III,**

Clinical trials

The requirements involved in research and also clinical trials and studies on patients are laid down in the Helsinki Declaration[5]. Section 21 of the Declaration of Helsinki lays down that such clinical trials may only be conducted if the purpose of the trials is so important that it outweighs the risks always inherent in any clinical trials. Clinical trials are ethically questionable if data or findings are already available which anticipate the potential trial results.

In view of this, there is a demand for extensive clinical trials before authorising medical devices, ideally randomised, to improve patient safety. This is currently required for all class IIb and III products, including by doctors' organisations[6].

Today's surgery and medical technology could not progress without research, development and team work. As far as research and development are concerned, the driving force here comes from the innovative spirit of manufacturers and users.

Working closely with leading surgeons, companies are continuously developing new products and investigating new surgical methods responsibly with patients in mind to optimise surgical treatment or even make it possible in the first place.

The new demands also put the basic principle of transferring technology from colleges and research establishments and the whole concept of thinking entrepreneurially is jeopardised.

Expensive and time-consuming clinical trials, which may take many years before any new products can be licensed, are feasible, but frequently cannot be justified in financial terms; monitoring the market carefully often makes more sense. And delaying launching new products for years also means patients often have to wait for life-saving technologies in vain.

The medical technology industry's assessment and proposed solution:

- The tendency of many politicians of treating class IIb and III medical devices as if they were pharmaceuticals must be refuted decisively. The effects of medical devices are predominantly based on physical principles, not on biological or pharmacokinetic ones.
- Medical devices in most cases are just one part of clinical methods. How safe they are, and what effects they have, depends like many surgical practices or other interventions very much on personal factors such as the surgeon’s skills, what technical equipment and infrastructure is available and how good the surgical team is working together.
- Many of the characteristics and effects medical devices have can be tested in the laboratory. Only if there are any biological or pharmacokinetic mechanisms involved can clinical studies be helpful.
- Using clinical studies to recertify medical devices which have already been successfully used in the market without any problems for years, even decades, is totally illogical and ethically unreasonable (see Declaration of Helsinki).

[5] WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, 2008
[6] ECRIN Petition 2013 (European Clinical Research Infrastructure Network)

- Especially with step by step innovations the improvements of individual steps tend to be small; comparative studies require very large numbers of patients to show such differences in statistically significant terms. Such considerable costs will delay ongoing quality improvements, or even eliminate them completely.
- Clinical trials should be limited to products which act via new mechanisms and/or those with biological or pharmacokinetic effects.
- Existing clinical data and experience need to be evaluated carefully, and could replace clinical trials in justified cases. Evidence of monitoring markets for at least three years should be regarded as equivalent to clinical trials.
- The path via literature data must remain open and possible in principle.

For more details of this aspect see Annexes II and III

Expected effects

With the present consideration, it will be provided a rational framework, based on examples from practice and on recognised national and international studies for the discussions on the new EU legislation proposal and to show those involved what effects their decisions will have.

This is not about reducing the rules to a minimum, but optimising them with a view to patient safety, whilst at the same time continuing to provide patients with a broad range of modern, affordable medical technology.

For more details of this aspect see Annexe IV

What is driving the costs in European healthcare systems?

- Additional European institutions or even new licensing authorities create hundreds of millions of Euros for each year. The additional costs for the notified bodies, national regulatory authorities and manufacturers together run into the billions. This is expected to cost the average hospital in Germany another EUR 200,000 or so and the average Dutch company around EUR 1 m a year[7].
- The effects of concentration will continue to increase healthcare costs and global competitive disadvantages for small and medium-sized enterprises (SMEs) in particular, which may put some of them at risk, as small companies have fewer sales over which they can spread their fixed expenses. Larger companies can also work in niche markets with smaller figures: such niche products will ultimately disappear from the market or the range of available variants will be limited. The products which remain will be marketed at higher prices, putting a burden on the healthcare system.

Regulatory pressure means less product diversity

- The wide range of versions available in medical technology up to now has enabled doctors to specifically respond to different anatomical characteristics and to individual forms of treatment. This growing product diversity has enabled the medical technology industry in recent decades to come very close to the goal of personalised medicine.
- Due to increasing costs for individual products manufacturers will need to reduce their range significantly and focus on what profitable products remain. The companies in the Tuttlingen area say this will mean a reduction of anything up to 30%.
- This means that many surgeons then will get their special instruments, which a priori cannot be beneficial for patient safety. This in particular will be the case in neurosurgery and in cardiovascular surgeries, where even simple products have to vanquish high licensing hurdles.

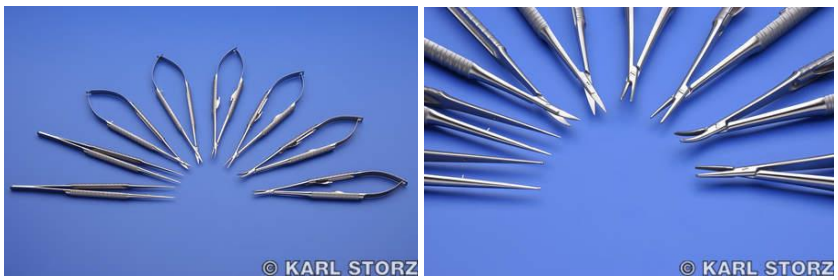

***Illustration**: Range of variations of micro-instruments from neuro- and vascular surgery*

The European medical technology industry as a global player

- European medical technology companies and German ones in particular, enjoy an outstanding reputation worldwide. They can roll out product innovations on the international markets promptly, which in recent decades has put them into a dominant position in many international markets (see Roland Berger, [Worldwide healthcare opportunities for Germany])

[7] MedicalMountains 2013; the quantitative differences are due to the different structures and sizes of hospitals involved

- Over-regulation, with products being licensed centrally (class IIb and III) and expensive and time-consuming clinical trials, puts innovative technologies back significantly (the industry estimates by around three years in Germany on average). This brings European medical technology companies in a much weaker competitive position.
- At the same time, delaying launching innovative medical technology means patients have to wait for lifesaving or supporting technology in vain.

CONCLUSIONS

With the present document, we ask that everyone concerned in the discussion and decision-making process in laying down the new European rules keeps a sense of proportion and involves not just the medical technology manufacturers, but also everyone working in the healthcare system in considering our patients' safety.

Only if everyone involved in providing services, from manufacturers through users to central processing, acts at the same high level of quality, we can optimise patient safety successfully.

As part of the industry, we see our contribution, but at the same time fear with some justification that the load will be devolved largely onto our shoulders. If the industry becomes over-regulated as expected, this will lead to significant adverse effects which will also undermine patient safety.

Annexes

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Annexe I: Classification rules

Rule 6 – first bullet point

Medical devices for cardiac surgery and cardiology: this may possibly merely be about accidentally omitting the word 'specifically'[8], but this has disproportionate consequences for many basic instruments which are upgraded to class III as a result.

Are there any foreseeable risks of failure?
› No

What this means is:
› Class III products are subject to the most stringent requirements; formerly, many such products were in class I.
› Some people are arguing they should only be marketed via (randomised) clinical trials.
› Particular mechanisms of the MDCG and potentially demands for re-licensing via a new European authority also take effect here.
› That would increase the costs involved disproportionately, but leaves patient safety unchanged; products will disappear from the market.

What reasons do there appear to be for this?
› None, mistake

Assessment and solution proposed:
› Insert the word 'specifically' and retain the existing established rule.

Rule 6 – second bullet point

According to some participants, thousands of *surgical instruments* will be upgraded from class I to class IIa by deleting this rule without replacing it. If we see reusable surgical instruments as an aid to assist surgeons in simple tissue manipulation (e.g. holding, clamping cutting, retracting etc.), upgrading them to class IIa is unjustified and pointless.

Are there foreseeable risks of failure?
› Surgical instruments have been developed over many decades, and are often named after the surgeons who developed them. Surgical instruments undergo a process of evolution, adapting their form, function and material characteristics to what surgeons and operating procedures need (**Annex**: Kocher arterial clamp).

What this means is:
› Class IIa products are monitored by a notified body. Complete range providers offer around 20,000 different instruments on average: in other words, this would affect an enormous number of products directly, with increasing audit times and costs as result.

[8] The analogous rule 7 governs this using the word 'specifically' as before

› Upgrading makes patients less safe, rather than more: the notified body's additional administrative costs involved would mean reducing the range considerably. MedicalMountain cluster companies expect the range to be reduced by 30%, so many surgeons will be unable to get the specific instruments they want.

› Suppliers would have to modify thousands of supply contracts and quality agreements.

What reasons seem to apply?

› Single-use (class IIa) and reusable (class I) surgical instruments are in different risk categories.

Assessment and solution proposed:

› Leave the status quo as it is, or

› Put single-use surgical instruments which do the same job as their equivalent reusable instruments in class I 'sterile' (Is).

› As the industry sees it, the main risk involved in using reusable instruments is due to reprocessing them correctly after they have been used. In recent years there have already been some improvements with the implementation of EN/ISO 17664; but we still see a considerable need for harmonisation in aligning different national rules in the clinics themselves. Some national manufacturers specify re-processing processes which cannot be used in other EU countries, for example.

› Other risks include products being repaired by unqualified persons[9] and exceeding the life cycles (aging) by the end-users.

› These statements are clearly supported by researching the literature for the keywords like 'surgical site infection'[10], forgotten surgical devices or consumables post-operatively[11], broken instruments[12] and medical technology's share of treatment errors[13].

[9] Spectaris: Problems relating to third-party repairs: Bringing the requirements for repair firms into line with those for manufacturers, 2013

[10] A study by Cornell University, New York puts the risk of infection during surgical intervention at 3% measured over all surgical interventions and up to 20% for emergency intra-abdominal interventions

[11] Studies by the US Departments of Health and Human Services put the number at approx. 1% of interventions. The Annals of Surgery put it at as much as 12.5%.

[12] An International Orthopaedics publication from 2002 puts the risk of instruments breaking during surgery at 0.03% for handheld instruments. For drills, the number is 0.14%.

[13] Medical technology accounted for 0.5% of the 3,932 treatment errors recognised as justified (treatment error opinion by the MDK community, annual statistics 2012, published by MDS – Medizinischer Dienst des Spitzenverbandes Bund der Krankenkassen e.V. May 2013)

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Rule 6 – third bullet point/rule 7 – second bullet point

Direct contact with the central nervous system (or even the central circulatory system as some are demanding) is not a sufficient criterion to classify medical devices as class III. We suggest using a wording in line with that for cardiac surgery[14] .

Are there foreseeable risks of failure?

› Not known

***Illustration**: Tissue spatula in neurosurgery. Source: KLS Martin Group*

What this means is:

› See above

What reasons seem to apply?

› The situation on guide wires should be included.

Assessment and solution proposed:

› Exclude basic instruments as per the wording proposed above.

New rule

Certain so-called 'closed-loop systems' should be put in risk category III.

Are there any foreseeable risks of failure?

› Not known.

What this means is:

› Many established, established systems combine therapeutic and diagnostic effects.

› This may also include insufflators and camera systems in endoscopy, navigation-controlled safety systems in surgery and other situations.

What reasons seem to apply?

› External defibrillators should be put in class III.

Assessment and solution proposed:

› Delete

[14] As in rule 6 first bullet point, i.e. **are intended <u>specifically to control, diagnose, monitor or correct a defect</u> of the central nervous system through direct contact with these parts of the body, in which case they are in class III,**

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Annexe II: Clinical trials

The Declaration of Helsinki[15] defines the requirements which should apply to research and also to clinical trials and patient studies. Section 21 of the Declaration states that such clinical trials may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects. Clinical trials are ethically questionable if data or findings are already to hand which pre-empt the potential study results.

This is why extensive clinical studies are demanded before medical devices are licensed, ideally randomised to increase patient safety. Some circles are demanding this for all class IIb and III products across the board, including doctors' organisations[16].

Are there any foreseeable risks of failure?

› The breast implant scandal, problems with hip prostheses

What this means is:

› An explosive increase in clinical trials with medical devices (class IIb, class III, all implants, others…)[17]

› Clinics are unprepared for this, either organisationally or in terms of capacity

› Burdening patients with unnecessary studies

› Clinical trials, which may take many years before any new products can be licensed, are feasible, but often cannot be justified in financial terms; monitoring the market carefully often makes more sense. And delaying launching new products for years also means patients often have to wait for life-saving technologies in vain.

› Having to recertify products which have been used in the market successfully and without any problems for years, even decades, is totally illogical and ethically unjustifiable.

Step by step innovation

› Especially with step by step innovations the improvements of individual steps tend to be small; comparative studies require very large numbers of patients to show such differences in statistically significant terms.

› The insuperable hurdles for the individual steps would make major successes achieved through the sum of many minor innovative steps together impossible.

› Medical devices are constantly changing and improving. Even at the end of clinical trials, improvements often become evident which sensible statutory regulation allows within certain limits. If this is interpreted narrowly, as is being discussed currently, it could lead to preventing such improvements or years of delays and considerable costs.

› Not allowing access to new therapies condemns patients to obsolete treatment, as we know from the USA[18] or Japan.

[15] WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, 2008
[16] ECRIN Petition 2013 (European Clinical Research Infrastructure Network)
[17] Around 320 new class III and 768 class IIb products are brought to market a year
[18] FDA Impact on U.S. Medical Technology Innovation (2010)

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What reasons seem to apply?

› Analogy with pharmaceuticals, demand for evidence, proof of benefits

Assessment and solution proposed:

› There are some fundamental differences between pharmaceuticals and medical devices:
  - Medical devices play only a minor role in many medical interventions (neurosurgical examining hook).
  - Unlike pharmaceuticals, many surgical and other interventions depend on personal factors, such as the surgeon's professional capability and experience, the technical equipment available (image quality, for example) how experienced the operating team is and how well they work together, and the infrastructure generally. All are points which run contrary to the concept of randomised controlled trials (RCTs).
  - Medical devices can be tested in the laboratory for many characteristics (all in some cases), while pharmacological effects can only be tested by cultivating cells and experimenting on animals to a very limited extent.

› Clinical data must be evaluated carefully; only if no comparable data is available are clinical trials necessary.

› The literature data route must remain open and possible in principle.

› Access to the market and the issue of refunds must be seen as two fundamentally different things.
  - Demanding comprehensive clinical evaluation of the benefits at the time of licensing puts the brakes on innovation.
  - Many medical devices play only a minor role in operating procedures (see above).
  - Cave: conversely, not evaluating the benefits (of the clinical method) in the clinical sense does not necessarily mean that such medical devices may not have any benefits. Their intended use defines the area in which they are used precisely; risk analysis reviews any potential problems carefully.
  - Demands to evaluate benefits clinically always relate to a method, not to the individual medical device concerned. That would burden those who manufacture a small proportion of a treatment method with aspects for which they are not responsible, which is not proportionate.

For the specifics of randomised controlled trials (RCTs) in indications that are rare, as they often are in the case of class III products, see **Annexe II.**

Annexe III: Randomised controlled trials (RCTs)

Randomised controlled trials (RCTs) are a successful way of comparing competing pharmaceutical therapies: so why are they specifically rarely the right way for innovative class III products?

- With RCTs, the clinical picture to be treated must be as uniform as possible, with as few differences as possible between individuals.
- There must be clear criteria for including and excluding patients; breaches of protocol must be rare exceptions.
- The effects of the intervention (success or failure) must be clearly recognisable and measurable
- If the effects of different interventions (such as different medications, for example) are to be compared, the influence of the doctor should be minimal
- The disease to be treated must occur frequently enough to be able to demonstrate the safety and efficacy of competing interventions within a limited recruitment phase and on enough patients.
- The intervention treatment involved (i.e. the pharmaceutical) must be present in its final form, and must not undergo any further changes (improvements).

These findings often do not apply to innovative medical devices for specific clinical pictures, such as intracranial aneurysms, for example

- Being included in a study also depends on ethical aspects of individual treatment options.
- Patients who would not have any treatment options otherwise are often treated especially in early phases. Most RCTs exclude patients whose prospects generally are poor.

How can we take the patient's interests into account and ensure their safety?

- RCTs do not prevent fraud or criminal dealings; the regulatory process must not impede the innovative power of medical technology!
- A sensible approach which balances patient safety and innovation against responsible business:
    - Companies must have thorough quality management systems
    - They and their products must be audited externally
    - Clinical data from market observation studies or registers

Annexe IV: Examples from practice

› Lazic, a family business from Tuttlingen, has been making aneurysm clips for decades, specialises in this field and is one of the world market leaders. The effects of the directive in terms of clinical trials for class III products would put its very existence at risk. Peter Lazic GmbH has sold approximately 210,000 aneurysm clips in total since the year 2000; there have been no near-incidents or incidents in that time.
Alternative methods of treatment, such as coiling in Europe, mean aneurysm clip surgery is a shrinking market, which is why there are now only a few aneurysm clip system manufacturers left, but the alternative treatment methods are not yet in a position to deal with all cerebral aneurysms, and the complexity involved means they will presumably not be within the foreseeable future. Should these methods become increasingly popular, however (as much as a 85:15 ratio for coiling), raising the licensing barriers too high could mean aneurysm clips vanishing from the market, leaving 15% of the patients involved with no alternative treatment option to coiling. Perhaps those patients will then seek treatment abroad, or not. So an established class III surgical system developed over decades could disappear from the market through over-regulation.

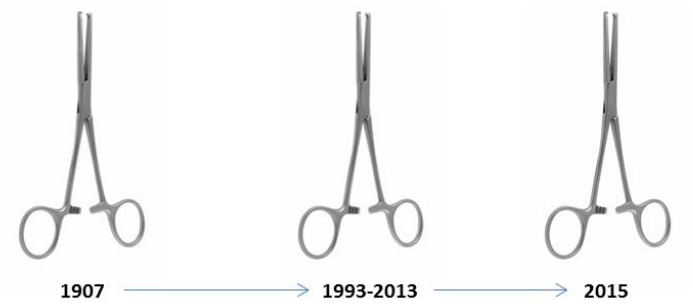
Aneurysm clip today (source: Peter Lazic GmbH)

› ADMEDES Schuessler GmbH Pforzheim, a young, innovative company, originally a spin-off of the famous KIT in Karlsruhe, says it would not have been founded if the licensing rules now being discussed would have applied 10 years ago. The company develops innovative products for treating otherwise mostly fatal neurovascular diseases.

› ZEPF MEDICAL INSTRUMENTS GmbH, Seitingen-Oberflacht, demonstrates by the example of a simple surgical instrument, known as the Kocher clamp, the decades of experience the company has with certain products.
The Kocher clamp has been on the market since 1907: it is a traumatic clamp, and belongs to the class of gripping instruments. It is used mainly when structures need to be grasped and held safely long-term, but should be compressed in the process (haemostasis/vascular ligature).

There are many companies which offer Kocher clamps; and the new EU Regulation would upgrade them from class I to class IIa. This would increase the additional certification costs involved for one and the same product many times over, which would not improve patient safety.

Kocher arterial clamps over time



Timeline		
Development	DIN 58232	No change
	EN/ISO 17664	No change
	DIN 980	No change
Reports/incidents	None	No change to risks
Risk category	I	IIa (proposed)
	93/42 EWG	New EU regulation
		Monitored by notified body
Applications		

7

erstellt: Robin Fox

› KARL STORZ GmbH & Co. KG, Tuttlingen, reports on the example of PDD for the different pace of medical device licensing in Europe and the USA. The medical devices we need to detect tumours at an early stage were licensed in Europe in 1995, but 15 years later in the USA, in 2010. The equipment had already progressed again by the time it was licensed in the USA: these benefits were quickly available to patients in Europe, but the USA needed a re-licensing process which took nearly two years. This method, which has been enshrined in the guidelines of the European Association of Urology (EAU) since 2005, has improved the diagnosis of cancer of the bladder and reduced the risk of recidivism.