

## Globalization of Medical Device Approval

A decade ago individual approvals for medical devices in each country were necessary – homologation in France, MedGV approval in Germany, MRS registration in the UK, and so on. Since then, EU-directives have been installed, and Mutual Recognition Agreements (MRA) between the EU and the USA, Canada, Australia, and New Zealand have been signed, enabling conformity assessment bodies of market A to approve devices for market B under the legislation of market B, and vice versa. In addition, the Global Harmonization Task Force (GHTF) was established to talk about real international harmonization in the approval of medical devices.

How far are we along the path to the globalization of medical device approval?

### Who is this news bulletin applicable to?

- Companies which manufacture and export private label medical devices and in vitro diagnostic medical devices worldwide.
- Companies such as OEM manufacturers which design, manufacture, and assemble medical and in vitro diagnostic medical devices, as well as suppliers, e.g. contract sterilization companies.

The speed at which approval of a new medical device for a foreign market can be gained is a crucial product success factor in today's competitive market environment.

TÜV SÜD Product Service enables an accelerated market entry for many countries through agreements with authorities and testing institutes.

Manufacturers benefit from being able to submit fewer documents or from consolidation of factory inspections.

### Have medical device approval regulations been harmonized within the EU?

Yes. The introduction of the Medical Device Directives since 1993 have harmonized medical device certification in the EU:

- Active Implantable Medical Devices Directive (AIMD)
- Medical Devices Directive (MDD)
- In Vitro Diagnostic Medical Devices Directive (IVD)

### What is the current situation in other major economic regions?

The approval is still very much regionalized and fragmented.

## **Eastern Europe**

Those Eastern European countries that did not join the EU in 2004 will continue to follow their own national procedures.

## **Russia**

Certification of a medical device in the EU does not simplify the registration process required in Russia. In addition to the registration, a device has to be safety tested by a nationally recognized test laboratory for GOST certification. Test results and auditing of medical device manufacturers by TÜV SÜD Product Service are recognized by our partners we work together with for the registration and GOST certification of your devices.

## **Switzerland**

Although situated in the heart of Europe, Switzerland still has its own legislation, but has harmonized it with EU certification regulations. An MRA has been signed between the EU and Switzerland, which includes the recognition of each other's certification of medical devices. Manufacturers outside the EU and Switzerland must have an EU representative within the EU, who is accepted by Switzerland unilaterally.

## **USA**

Medical devices in class I and II requiring clearance for US market entry can only attain acceptance via a pre-market notification procedure, otherwise referred to as 510(k). The term 510(k) originates from section 510(k) of the Federal Food, Drug, and Cosmetic Act. A 510(k) submission is based on comparison of the new device with devices already legally marketed in the USA, which allows the US Food and Drug Administration (FDA) to determine whether a

device is safe and effective. Medical device manufacturers are required to submit a 510(k) if they intend either to introduce a device for commercial distribution in the US for the first time, or to reintroduce a device that has been substantially modified. 510(k) was previously conducted by the FDA only. Starting in 1996, the system was revised to allow several third-party testing institutes to carry out the administrative and substantive review of the documentation on behalf of the FDA and to allow a faster and more efficient market access. TÜV SÜD Product Service was already authorized by the FDA in 1996 to perform third party reviews for all eligible devices. So far we have successfully performed more than 200 third party reviews under the US FDA Accredited Persons Program. The advantage for you is direct contact and communication. The timeline is 30 days for our review and another 15 days for the final FDA review. The final review is comparable to the FDA internal procedure. Furthermore their reviewer has to forward his/her recommendation to the supervisor for final decision. The FDA fee of about USD 4.150,- is only relevant if you submit the 510(k) directly to the FDA.

After product approval, the FDA can carry out a production site inspection at any time. As a rule, this takes four working days and encompasses management, development, corrective and preventive action, as well as production and process control.

Under the mutual recognition agreement between the EU and the USA (MRA) and also under the FDA's Modernization Act, manufacturers can have routine inspections done by TÜV SÜD Product Service combined with an audit under

EU regulation. When the FDA announces the inspection you may respond to the FDA that you would like to participate in the Accredited Persons Program. In this case you should contact us. We also offer pre-audits based on the FDA regulations.

Moreover, TÜV SÜD Product Service is a National Recognized Testing Laboratory (NRTL) for the US market and offers to test your device according to e.g. UL 60601-1. The basis for NRTL medical product certification is the testing of electrical and mechanical safety according to IEC 60601-1. You can get a complete testing package including factory inspections from one partner. If you are already a customer in the context of system certification, a yearly audit can be combined easily and cost-effectively with one of these factory inspection.

In addition, we will test your device according to the US-specific EMC requirements.

### **Canada**

The Canadian Medical Devices Regulations Statute recognizes four categories of medical devices, similar to the EU Medical Device Directive, a difference being that Canadian law integrates IVD products and active implants. Since 1 January 2003, Canadian law requires that manufacturers of class II, III, and IV medical devices and IVD devices have a quality management system that meets the requirements of ISO 13485 in order to obtain a license to sell their devices in Canada. Only a CMDCAS certificate issued by a SCC accredited CMDCAS registrar will be accepted. Manufacturers of medical devices licensed for sale in the Canadian market have to renew their device licenses

annually until 1 November and therefore need to submit a copy of their CMDCAS certificate.

TÜV America Inc. was the first registrar accredited by the Standards Council of Canada (SCC) to perform ISO 13485 CMDCAS certification.

Over 70 specially trained and authorized auditors from TÜV America and its sister company TÜV SÜD Product Service ensure CMDCAS certification for all clients.

We pre-review your device license application regarding compliance with the requirements of the Canadian agency TPD (Therapeutic Products Directorate).

TÜV SÜD Product Service is also authorized for the Canadian market as NRTL for the standard CAN/CSA-C22.2 Nr. 601.1.

### **Brazil**

The requirements for the medical device registration are harmonized with the other member states of MERCOSUR. The documentation to be submitted is to a large extent compliant with the Global Harmonization Task Force (GHTF) Guidance for Summary of Technical Documentation (STED). Testing and certification by a nationally recognized certification body is needed for electrical medical devices to achieve market access in Brazil. Tests performed by TÜV SÜD Product Service are fully recognized by Brazilian test houses we cooperate with. The related yearly factory inspections can be performed by TÜV SÜD Product Service, i.e. within the framework of the EU Notified Body audits.

## Japan

The revised Japanese Pharmaceutical Affairs Law (PAL) became effective on 1 April 2005. There are four classes of medical devices. The quality management system conformity criteria for manufacturing facilities of medical devices and in vitro diagnostic reagents are assessed prior to device approval and/or device certification. Not only the manufacturing facilities in Japan, but also those overseas must fulfill the GMP rule, based upon ISO standard 13485:2003. Class I products are exempt from the obligation for certification. Class II medical devices are certified by Registered Certification Bodies (RCB) as long as conformity certification criteria in the form of JIS standards are assigned to the devices. Products with a higher risk potential still need approval by the Pharmaceuticals and Medical Devices Agency (PMDA). For Class II devices, a product documentation in accordance with the Global Harmonization Task Force (GHTF) Guidance for Summary of Technical Documentation (STED) has to be submitted to the Japanese RCB. In addition to previous documents, detailed information on the company must also be provided. An audit is to be carried out by the RCB in accordance with Japanese GMP requirements (ISO 13485:2003) before device certification. For products in higher classes this responsibility is assumed by the PMDA. In this case an assessment, but not inevitably an audit, is required. The extent to which GMP audits of the RCB are recognized by the PMDA for class III and IV device approval applications is not yet clear. However, manufacturers of such devices have already been audited by TÜV SÜD Product Service to demonstrate compliance with GMP requirements.

TÜV SÜD Japan has many years of experience and holds the deputy chair in the committee for the RCBs. Take advantage of our service as RCB.

PMDA requires tests for class III and IV devices according to JIS standards to be performed by recognized test laboratories such as TÜV SÜD Product Service. We also offer to test your device according to the national EMC requirements.

## China

There are two different schemes for approval of medical devices in China: SFDA (State Drug Administration of China) registration and CCC (China Compulsory Certification). The SFDA registration covers all kind of medical devices marketed in China, while the CCC is only required for seven categories of medical appliances (1. Medical diagnostic X-ray equipment, 2. Haemodialysis equipment, 3. Hollow fiber dialyser, 4. Extra-corporeal blood circuit for blood purification equipment, 5. Electrocardiograph, 6. Implantable cardiac pacemaker, 7. Artificial heart-lung machine). SFDA classifies medical devices into three categories according to their risk potential. The registration of class II and III devices generally requires testing by recognized test laboratories. In the case of class III devices, the SFDA performs a factory inspection every four years. Tests done by TÜV SÜD Product Service are partly recognized, according to prior agreement, by the Chinese test houses. TÜV SÜD Product Service is authorized to evaluate the application and to submit it to SFDA. We clarify the extent of additional testing for you and coordinate the testing at a recognized national test house.

The existence of a CCC mark is checked by customs at market entrance. The CCC is handled by the China Quality Certification Center (CQC), a subsidiary of the State General Administration for Quality Supervision and Inspection and Quarantine of the People's Republic of China (AQSIQ). Tests need to be carried out in China.

CQC will organize the factory inspection and decides when and by whom the inspection should be performed. The manufacturer may provide a proposal for the authorized organization which performs the inspection, e.g. TÜV SÜD Product Service.

### **Taiwan**

For registration of medical devices in Taiwan, the Pharmaceutical Affairs Law (PAL) applies. The Ministry of Health handles particular definitions and charges official organizations with implementation. Manufacturers wishing to export to Taiwan must, among other things, submit a detailed company description, a description of the production process, and a quality system documentation (QSD) including work and test instructions. A cooperation between the EU and Taiwanese authorities exists, which facilitates accelerated market access for medical devices. On this basis TÜV SÜD Product Service played a major role in the negotiations and the implementation of a private agreement with the Taiwanese certification bodies. An audit by TÜV SÜD, which includes the Taiwanese regulations, plus certification under ISO 13485, the quality management standard for medical product manufacturers, the audit report, and a Free Sales Certificate suffice for the GMP compliance letter, the required basis for registration of products in Taiwan. This GMP compliance letter from the DoH in Taiwan is valid for three years. This document forms one part of the records to be submitted for any medical device registration. The application can only be performed by your representative in Taiwan, not by the foreign manufacturer. Since November 2003 TÜV SÜD Product Service is authorized to perform this kind of audits.

As a prerequisite, the devices relevant to the Taiwanese market were covered at the audit under ISO 13485. The quality management system ensures that only devices registered with the Taiwanese DoH are delivered to Taiwan.

There has to be an agreement with a Taiwanese distributor addressing market surveillance and reciprocal information of any complaints.

After a successful audit we issue an audit report confirming the compliance with Taiwanese regulations and reference to the agreement with Taiwanese certification bodies. This replaces the submission of a QSD. In most cases an additional audit is not necessary. In any case evidence needs to be provided regarding the handling of vigilance and distribution and to be evaluated by the lead auditor for your company.

### **Australia**

The amendment to the Therapeutic Goods Act and the new regulations took effect on 4 October 2002. Products that have not yet been registered under the new procedures, may no longer be placed in the market. Australia has implemented the model developed by the GHTF. The regulations and the approval process correspond substantially to the requirements within the EU. Nevertheless, for companies that do not apply the MRA between Australia and the EU, a complete registration process must be carried out. TÜV SÜD Product Service is authorized within the MRA as a conformity assessment body (CAB) and offers an abbreviated registration process at a favorable cost.

With the AUS-EU MRA certificate we offer, the AUS TGA incorporates devices into the Australian Register of Therapeutic Goods (ARTG) within five working days. For this purpose, your Australian sponsor needs to submit the MRA certificate, application form, copy of labeling, copy of Australian conformity declaration, and a copy of the EC and ISO certificates to the Therapeutic Goods Administration (TGA). Otherwise it currently takes between two months and one year for the TGA to decide to carry out an audit. Using the MRA for the

registration process, there is no audit carried out by the TGA, no additional assessment of the technical file, no consultation with the national health authority and no charges connected to this are necessary.

The following documentation is required under the AUS-EU MRA to be reviewed prior to the issue of an AUS-EU MRA certificate:

- EC and ISO certificates for the devices concerned
- last audit report issued by certification body
- test reports, if not available at TÜV SÜD Product Service
- product labeling (labels, user manual, advertisement)
- device description (technical drawing (only overview), technical description)
- essential requirements checklist
- risk analysis summary
- clinical data summary, if not available at TÜV SÜD Product Service
- declaration of conformity according to Australian regulations

**Our services with global impact are described on the last page.**

### **Are these different approval schemes mutually recognized?**

Partly, yes. Mutual Recognition Agreements (MRA) have been signed between the EU and the US, Canada, Australia, and New Zealand. The purpose of an MRA between markets A and B is to allow conformity assessment bodies (CAB) of market A to approve devices for market B under the legislation of market B and vice versa. Each market retains its own legislation and approval scheme, but the access is simplified by opening the system to foreign CABs.

### **Doesn't this mean that even with MRAs, manufacturers still have to fulfill several approval systems?**

With this scheme, manufacturers may still have to fulfill several approval systems with different requirements, but at least all procedures can be registered and certified by a single body in the manufacturers' home country.

### **Is there any international body working towards true harmonization of approval requirements?**

Yes. The Global Harmonization Task Force (GHTF) was set up in 1993 with the aim of achieving harmonization in medical device regulatory practices. This voluntary group has members from the EU, USA, Canada, Japan, and Australia. The purpose of the GHTF is to encourage convergence on regulatory practices related to ensuring the safety, effectiveness/performance and quality of medical devices, promoting technological innovation, and facilitating international trade. The primary way in which the GHTF works is to publish and disseminate harmonized guidance documents on basic regulatory practices. These documents which are developed by five different GHTF Study Groups can then be adopted/implemented by the members' national regulatory authorities. TÜV SÜD Product Service also participates in various working groups of the GHTF.

### **What has the GHTF harmonized to date?**

There are a number of harmonized regulatory components which together form the global regulatory model. Among these components are: essential principles for safety and performance; labeling of medical devices; the role of standards; summary of technical documentation; classification of medical devices; and a set of

documents used for the vigilance reporting system. As quite a number of these harmonized documents have been derived from the European regulatory system, there is already a high congruence between the European legislation and the global regulatory model. The table shows some of the final documents which are congruent with the EU regulation.

**Link to informative website:**  
<http://www.ghtf.org>

**Does this mean that these GHTF/EU documents will be implemented in the US, Japan, etc.?**

As time goes by, with every modification of one of these regulations it can be expected that a further

step is taken towards the global regulatory model. As these steps are within the sovereignty of each country, it is clear that no termination date for that process can be given. Partial implementation took place in Australia and Japan. In the USA a pilot program was established at the FDA.

**Will the GHTF manage to harmonize all regulations and procedures, and if so, when?**

The GHTF can only process a target point for global harmonization so that global regulatory model might be completed within a few years. The “real” harmonization will take place when sovereign countries accept this model and adapt their own national regulations accordingly.

<b>GHTF Guidance</b>	<b>EU Regulation</b>
SG1-NO20R5:2000-10-23 Essential principles of safety and performance of medical devices	MDD, AIMD (Annex I in both Directives)
SG1-N009R6:2000-10-23 Labeling for medical devices	MDD, AIMD (Annex I in both Directives)
SG1-NO12R10:2000-10-23 Role of standards in the assessment of medical devices	MDD, Article 5 AIMD, Article 5
SG1-NO11R17: 2003-12-16 Summary technical documentation for demonstrating conformity to the essential principles of safety and performance of medical devices (STED)	MDD (Annex II.3, VII), AIMD (Annex 2.4)
SG4(99)28:2000-10-30 Guidelines for regulatory auditing of quality systems of medical device manufacturers – part 1: general requirements	MEDDEV 2.05/2 Rev. 3:06-1999

[www.tuev-sued.com/mhs](http://www.tuev-sued.com/mhs)

### **Our services with global impact**

TÜV SÜD Product Service is a National Certification Body (NCB) and, within this scope, tests medical devices in compliance with applicable IEC standards; it can issue a CB report and a CB certificate. With these documents it is possible to acquire national certificates and approvals offered by certification bodies participating in the CB scheme – at present in more than 40 countries – in an abridged and therefore cost-effective and swift manner.

Further support for your export activities is available in the form of a Free Sales Certificate which is issued on request. Some non-EU countries require such documents as proof of compliance with national standards as well as as a confirmation paper for legal sales on the domestic market.

### **Why TÜV SÜD Product Service?**

- National Certification Body able to issue a CB report and CB certificate
- Prompt service – saving precious time-to-market
- Key market approvals from one partner – saving you money!

Regardless of whether it concerns USA, Australia, Taiwan, or another market: Detailed knowledge of market approval routes is imperative for securing speedy and cost-effective time-to-market. TÜV SÜD Product Service experts can offer the medical device manufacturer crucial support based on long-term experience and cooperation agreements in this field.

Your contact partner at TÜV SÜD Product Service can give you further information.

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