Regulation of orthopaedic implants : two systems compared

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Introduction

In many countries laws have been drafted in order to protect public health against unsafe medical devices. Medical devices comprise a variety of products, for instance bandages and syringes but also more dangerous products like pacemakers and artificial heartvalves. Orthopaedic implants are also medical devices.

The regulatory system for medical devices in the United States is one of the oldest and most stringent in the world.

In Europe, the systems vary between the countries. Some governments employ a system in which a device must have obtained government approval before it is allowed on the market. Other systems focus on control of the manufacturing process. In some countries the law applies only to specific categories of medical devices.

However, there are also countries with very limited regulation or no regulation at all. The dangers of a situation without regulatory requirements are obvious. The following statement was made in the United States before the Medical Device Amendments were enacted:

> *" ...under current standards of nonregulation in the United States, I could take a paperclip and fashion it into an IUD. I could begin inserting it into women without even informing them that it is an experimental and never-tested IUD, and I would not even have to inform the FDA of my newly invented IUD."*[1]

Since the mid 80's, the European regulatory systems have been object of harmonisation proposals. In order to realize a common market by 1992, all trade barriers between the member states should be abolished. For medical devices, trade barriers comprise different regulatory requirements with respect to market entrance. These national requirements should be replaced by common requirements as laid down in European Community directives.

The objective of quality legislation will be protection of the safety of the patient. "Overregulation" will cause negative effects, for instance on innovation; new developments which are beneficial to the patient may be stopped by rigid regulatory requirements. On the other hand, a system with no regulatory control at all will allow all devices on the market regardless of the fact whether there is evidence regarding safety and effectiveness.

We will compare a system with very detailed legal requirements for orthopaedic implants (the United States' Medical Device Amendments) with the future system of the European Community which will eventually be implemented in each European Community member state. This new system will end the situation of "unregulated" member states.

The United States

In 1976 the Medical Devices Amendments were enacted in

1 Testimony of Dr. R.J. Thompson, Silas B. Hayes Army Hospital at Ford Ord, as cited in the Senate Committee Report on the Medical Device Amendments of 1976, 94th Congress Report No. 94-33.

the United States.[2] Safety and effectiveness of medical devices had become a matter of public responsibility. The introduction of the Amendments meant a tremendous challenge for the United States Food and Drug Administration (FDA). The requirements concern about 1800 different types of medical devices, marketed by about 7000 manufacturers and distributors. Altogether the FDA supervises about 41000 products, varying from "bedpans to brainscans".[3] Generally considered, the Amendments are "complex legislation negotiated by lawyers for lawyers".[4]

The objective of the Amendments is "to establish a mechanism in which the public is afforded reasonable assurance that medical devices are safe and effective".[5] Effectiveness is in the first place explained as the reliability over time of a medical device, but also has to be weighed "any probable benefit to health from the use of the device against any probable risk of injury or illness from such use". The Amendments contain specific provisions setting forth how effectiveness is to be determined: effectiveness is to be determined on the basis of well-controlled investigations by qualified experts, including clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device.[6] From these investigations should fairly and responsibly be concluded that the device wil have the effect it purports or is represented to have under the conditions of use prescribed.[7]

The Medical Device Amendments require that devices be classified into one of three classes, depending on the extent of regulation necessary to assure safety and effectiveness. The requirements are more stringent depending on the risk associated with the use of the device.

After the enactment of the Medical Device Amendments, the FDA started classifying medical devices in the various classes. Because of the registration and listing obligation, manufacturers have to notify the FDA that they intend to bring a medical device, for instance an orthopaedic implant, on the market (the so-called "premarket notification provision", Sec.510(k) of the Medical Device Amendments). Subsequently, the FDA will consider whether the notified device is "substantial equivalent" to a preamendment device. The conclusion "substantial equivalence" is no proof of safety and effectiveness, but solely a statement that the device in question is not less safe or effective than a comparable pre amendments device. If "substantially equivalence" is accepted, the device is directly admitted to the market. If not, classification in class III follows automatically and the device is submitted to a PMA procedure, unless a request for reclassification to class II or I is met. Premarket approval means that the safety and effectiveness of class III devices (pre or post amendments) has to be proved on basis of "valid scientific evidence". As

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2 Medical Device Amendments of 1976, Pub.L. No. 94-295 (1976), 90 Stat. 539 (codified at 15 US C par. 55 and 21 US C passim), Chapter V of the Federal Food, Drug, and Cosmetic Act of 1938 and 21 Code of Federal Regulations, parts 800 to 1299.

3 Staff of House Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce, 98th Cong., 1st Sess., Report on Medical Device Regulation: The FDA's Neglected Child 1 (Comm. Print 98-F 1983).

4 Munsey, R.R. and Samuel, F.F. Jr. (1984); Medical device regulation, in transition; 75th Anniversary Commemorative Volume of Food and Drug Law, (the Food and Drug Law Institute, ed.), pp. 350-379; Food and Drug Law Institute Series, Washington D.C.

5 United States Congress, House of Representatives; Report to accompany H.R. 11124, Medical Device Amendments of 1976, 94th Congress, 2d session, Report No. 94-853.

6 Mark that effectiveness is used in the meaning of "efficacy". Hence the Federal Food, Drug and Cosmetic Act uses the terms indifferntly.
Gelijns, A.C. (1991); Innovation in clinical practice, the dynamics of medical technology development; National Academy Press, Washington, D.C.
Bunker, J.P. (1988); Is efficacy the gold standard for quality assessment?; Inquiry 25, pp. 51-58.

7 Medical Device Amendments 1976, Sec. 513 (a).

a consequence, clinical trials will have to be carried out with the device.

European Community Directives

In the European Community, in the various member states, approaches to quality regulation of medical devices tend to differ. For a manufacturer this means that his medical device has to meet a variety of requirements, depending on the country where he wants to market his device. Differences may include different labelling requirements, different registration-methods or different Good Manufacturing Practices for instance. These provisions are, with regard to the principles of basic community law, "barriers to trade" and should be abolished. They are conflicting with the objective to create a common market in the European Community before 1993.[8] In order to realize this objective, a harmonisation policy is being drafted. The EC-policy for medical devices implies that after 1992 a device which is admitted to the market in one member state, will immediately have access in all other countries, without additional demands.

Medical devices are classified as industrial products and trade restrictions will have to be removed in the same way as with regard to other categories of industrial products.

Hence, the applicable system of harmonization in the field of industrial goods, the so called "New Approach" will apply to medical devices as well.[9] This approach is based on the principle that harmonization will be limited to the adoption, by means of directives, of the most important safety requirements ("Essential Requirements") products on the market have to meet in order to be allowed in free trade in the Community. Normalization-institutions are assigned to draft technical specifications ("standards"). "CEN" and "CENELEC" are presently charged with the drafting of European standards.[10] Trade and industry need these specifications in order to meet the "Essential Requirements" as they are required in the directives. However, these standards are not binding. The manufacturer may prove compliance of his products with the "Essential Requirements" by referring to European standards or in an other way as described in the directive.

On the European Community level four manufacturers' trade-organisations are involved in drafting three directives which will constitute the basics of this harmonisation policy. Medical devices are divided into three product groups and for each group a separate directive will be drafted.

The directive regarding "the active implantable electro-medical devices" (AIEMD) is the first and it has, in draft, been accepted by the European Commission.[11] The second directive covers a variety of medical devices, either

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8 Article 2 of the treaty (Treaty in order to institute the European Economic Community, signed in Rome, March 25, 1957) describes the objectives of the European Economic Community: "harmonic development of the economic activity within the whole of the Community, a steady and balanced expansion, a greater stability, an increasing improvement of the standard of living and closer relations between the States united in the Community". These objectives should be reached by: "the institution of a common market and the gradually drawing nearer to each other of the economic policies of the Member-States". In order to attain the objective of one common market, all barriers to trade should be abolished between the member states. The completion of the internal market is more in detail described in the "Single European Act" which came into force in July 1987. This treaty is an amendment to the Treaty of Rome (basis for the European Community: the European Community treaty) and its goal is the accomplishment of the common market by December 31, 1992.

9 In 1985 the European Community Council accepted a resolution regarding a new approach in the field of technical harmonization and normalization (Council Resolution, May 7, 1985, European Community Publication Journal, Nr. C 136). In this resolution a policy was mapped out, the so-called "New Approach". This policy is based on a decision by the European Court in which it was decided that a product manufactured and marketed in accordance with the requirements of one member state, must be admitted in all other member states (Case 120/78, "Cassis de Dijon").

10 CEN: European normalization committee and CENELEC: European Committee for electrotechnical normalization.

11 Official Journal of the European Communities L 189 of 20 July, 1990.

electromedical (but not implantable) or not. An official Commission proposal is expected early in 1991. The draft proposal was published in 1990.[12] The third directive covers in vitro diagnostic devices. A draft version on this directive is not expected before the end of 1991.

A general requirement in the directives is that medical devices placed on the market will "not compromise the safety and health of patients, users and other persons when properly installed, maintained and used in accordance with their intended purpose."[13] What safety means is explained in detail in the "Essential Requirements". Manufacturers must meet these requirements if they want to market their device. The requirements are technically specified in harmonized standards. As explained above, these standards are voluntary. This means that a manufacturer may prove compliance to the "Essential Requirements" by manufacturing in accordance with these standards. He may also choose to do this in an other way.

The medical devices subject to the the second directive, the socalled "Directive on medical devices", are classified in classes. In an annexe of the directive, classification decision criteria are described. The classification is considered upon the risks involved in using the device. Under "use" is *understood using according to the manufacturer's* directions and intentions. The three-classes system is meant to impose requirements relative to the risk.

To the low risk class (class I) belong devices like dressings and wheelchairs which, if used in accordance with the intentions, "do not present a foreseeable risk of irreversible illness or injury".

In class IIa and IIb ("intermediate risk") devices are classified which may cause such a risk. However, these devices do not cause risk of "death or serious irreversible illness or injury". Orthopaedic implants will be classified into class IIb. Devices classified in class III, "high risk" devices, present risk of death or serious damage. Artificial heart valves, for example, belong to this class.

Conclusion

If we compare the two systems, we notice that they have *different objectives:*

United States:	"To provide reasonable assurance of the safety and effectiveness of the device"
European Community:	"A device should not compromise the safety *and health of patients*".

In the United States, the system is very detailed with many specific requirements regarding a wide spectrum of objects: research and development, the manufacturing process, market introduction and post marketing surveillance. Safety as well as effectiveness of the device are emphasized. However, soon after enactment of the system it became obvious that it would be very difficult to enforce the system as intended by Congress. Budgetary problems combined with the tremendous amount of devices to cover, were the reason of all these troubles.[14] Another issue in this respect is the fact that only 10% of all medical devices are class III devices for which the manufacturer has to prove safety and effectiveness through "valid scientific evidence" by

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12 Commission of the European Communities (1990); Draft Proposal for a Council Directive on medical devices; Brussels, 15 July 1990.

13 Commission of the European Communities (1990); Draft Proposal for a Council Directive on medical devices; Brussels, 15 July 1990.

14 Staff of House Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce 98th Cong., 1st sess., (1983); Report on medical device regulation: "the FDA's neglected child"; Comm. Print 98-F; Washington, D.C.

conducting clinical trials. There and above, 90% of all devices enter the market through the 510(k) route, meaning that the manufacturer proves substantial equivalence to a device already on the market. In that case there is not a specific requirement to conduct clinical trials with the device. Hence, effectivenesss is no longer a legal requirement.

The (future) system of the European Community focuses on safety and not on *effectiveness* of the medical device. As a consequence, a perfectly safe medical device may be brought on the market that does not have any effect on the health of the patient. At this moment it is too early to comment on the functioning of the European Community medical device quality policy as it is still in the process of being drafted.

If we compare the two systems, it is clear that both the system of the Medical Device Amendments and the future system of the European Community focus on the safety of product and the manufacturing process. In both systems the establishment of *effectiveness* is in most cases left to the health care professional and manufacturers or, nowadays often to reimbursement parties.[15,16]

As a consequence, in most cases assessment regarding efficacy and effectiveness will take place (if it takes place at all) in the post marketing stage. This should not be seen as a negative aspect: several authors state that premarketing clinical trials will not detect complications that will occur in daily practice.[17] Therefore attention should be paid to post marketing surveillance. In the United States in the most recent changes to the Medical Device Amendments, the Safe Medical Devices Act of 1990, a specific provision is enacted regarding post marketing surveillance of risky and critical devices (for instance orthopaedic implants) first introduced into commercial distribution after January 1, 1991. It is not exactly clear what the FDA will require as post marketing surveillance. It may include a post marketing surveillance study but also the reporting of adverse incidents. In the European Community system post marketing surveillance relates in the first place to the reporting of adverse events.

If the emphasis shifts in both systems to the post marketing stage, it is obvious that determining efficacy and effectiveness can only be done through true efforts of the health care professionals themselves. Active participation in quality assurance projects, for instance, multi center trials, will be required in this respect.

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15 With the exception of the American Class III devices which are not substantially equivalent to already marketed devices and the European Community Class III devices.

16 Insurers increasingly ask for evidence of efficacy as a condition for reimbursement.

17 Gelijns 1991 and Bunker 1988.