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**Self-Testing and Self-Monitoring  
of Oral Anticoagulant Therapy:  
Consensus of the Italian Federation  
of Anticoagulation Clinics**

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**Self-Testing and Self-Monitoring  
of Oral Anticoagulant Therapy:  
Consensus of the Italian Federation  
of Anticoagulation Clinics (F.C.S.A.)**

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## Self-testing and self-monitoring of oral anticoagulant therapy: consensus of the Italian Federation of Anticoagulation Clinics

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### 1. Scientific background

Oral anticoagulation therapy (OAT) is a life-saving therapy used by over 500,000 people in Italy. The purpose of the therapy is to induce controlled blood anticoagulation in order to prevent the appearance of thrombosis in patients at risk. The indications for OAT are numerous because thrombosis, especially of the cerebral and coronary arteries, is the first cause of death in Italy. The indications include atrial fibrillation, cardiac prostheses and valvular disease, embolic cerebral ictus and venous thromboembolism (FCSA Guide 2002). The risk of thrombosis increases with age and the progressive aging of the population is causing a constant increase in the number of patients that need OAT. Effective management of this therapy is therefore a health problem of primary social and economic relevance.

#### 1.1 Oral anticoagulation therapy management models

The effectiveness of OAT and its safety strictly depend upon maintaining a proper degree of anticoagulation, that is a proper *therapeutic range* expressed as *PT INR* (*Prothrombin Time, International Normalized Ratio*) (FCSA Guide 2002). An excess of anticoagulation (that is, a PT INR above the therapeutic range) exposes the patient to a high risk of hemorrhages, while on the other hand, low anticoagulation does not protect the patient from the risk of thrombosis. Several studies proved the importance of maintaining a proper therapeutic range (Hylek 1994, Cannegeter 1995, ASPECT Research Group 1994). An analysis of the primary prevention trials of atrial fibrillation proved that the majority of both hemorrhagic and thrombotic complications occurred when the PT INR was out of the therapeutic range and that both the effectiveness of OAT and its safety increased when good control of the anticoagulation level was maintained (Albers 1994). The Italian Federation of Anticoagulation Clinics carried out a prospective multicenter study of the hemorrhagic and thrombotic complications of OAT in Italy; 34 clinics across the whole nation were involved. During this study, more than 2,700 patients were followed from the beginning of their anticoagulation treatment for a total follow-up time of more than 2,000 patient-years (pt-yr). The hemorrhagic complications were particularly frequent when the PT INR was greater than 4.5 (40.5% pt-yr) and much less frequent when the PT INR was within the therapeutic range (4.8% pt-yr) (Palareti 1996).

The incidence of thrombotic complications was 17.5% pt-yr when the PT INR was < 1.5, and 2.3% pt-yr for values of PT INR between 2.0 and 3.0 (Palareti 1997). Good management of OAT is therefore indispensable.

A number of different OAT management models exist. The model that prevails in the United States is called *Usual Care* (UC): patients are generally followed by their general practitioner or by a specialist. The *Anticoagulation Clinics* (AC) model, that is Clinics specialized in monitoring OAT, prevails in many European countries, especially in the United Kingdom, Holland and Italy. There is growing evidence in the literature that AC allow better OAT control and therefore lower incidences of hemorrhagic and thrombotic complications (Ansell 2001). Non-randomized comparative studies (Garabedian-Ruffalo 1985, Cortelazzo 1993, Wilt 1995, Chiquette 1998) showed that the frequency of severe bleeding due to OAT was between 0 and 2.4% pt-yr for patients followed in AC, whereas it was to 3.9 to 17.8% pt-yr in patients followed with UC. Likewise, the frequency of therapeutic failures, that is of thrombotic complications in spite of OAT, was much lower in the AC than in the UC (0–3.5% pt-yr vs 6.2–42.8% pt-yr). In financial terms, considering the costs saved by avoiding complications, AC account for a global saving of about 1,000 to 4,000 dollars for therapy year-patient (Ansell 2001). There are many reasons why AC can manage OAT patients particularly well. Among the most important reasons, are the accurate laboratory PT INR checks, a structured network for managing emergencies and complications, including minor ones; and, in general, an organized system of continuous education, communication and follow up of the patient. Today, AC therefore represent the reference standard for OAT management and new possible therapy control systems such as self-monitoring will have to be compared to AC.

#### 1.2 Self-monitoring of oral anticoagulation therapy

OAT self-monitoring with portable coagulometers is a new therapy management model that has the potential advantage of being more convenient for the patient and possibly of improving monitoring quality and of further reducing the frequency of complications. There are several ways of using portable coagulometers; for the sake of simplicity, we will summarize them as *self-testing* and *self-management*.

### 1.2.1 Self-testing

With *self-testing* the patient autonomously monitors his/her own PT INR using the portable coagulometer, leaving OAT decisions to his/her general practitioner, specialist or anticoagulation clinic. Self-testing therefore offers the patient the opportunity of increasing the test frequency every time this is deemed to be necessary.

In a short, randomized and controlled study, White *et al.* evaluated the patients' ability to measure their own PT, while the drug dosage was managed by their physician (White 1989). The 23 *self-testing* patients remained within the therapeutic range for more time than did the control group of 23 AC patients (time spent within the range 87% vs 68%,  $p < 0.001$ ).

The study was too limited to evaluate possible differences in the incidence of hemorrhagic and thrombotic complications between the two groups.

Anderson *et al.* confirmed the feasibility of self-testing and estimated its accuracy in a prospective cohort of 40 patients who monitored their therapy at home over a period of 6–24 months (Anderson 1996). The average degree of agreement between the PT measured by the patient and the reference one was between 83 and 96% ; 97% of the patients stated that they preferred self-testing to traditional monitoring. Likewise, Andrew *et al.* analyzed the use of a portable coagulometer by 82 adults and 11 children (Andrew 1996). No significant difference was observed between the PT INR values measured by the patients and by the laboratory (correlation degree  $r = 0.92$ ). Also in this study, 95% of the patients preferred using the portable coagulometer to the laboratory test. Beyth and Landefeld randomized 325 elderly patients from the beginning of their OAT (Beyth 1997). For 163 patients, dosage was determined by one of the researchers based on the PT INR measured at home by the patients (*self-testing* arm); for the remaining 162 patients, dosage was determined by their physician based on the PT INR measured by the laboratory (*usual care* arm). Over a period of 6 months, the researchers observed a 5.7% frequency of major hemorrhages in the *self-testing* group vs 12% in the *usual care* group. In Italy, Cosmi *et al.* studied 78 patients on stable OAT who measured their PT INR at home with a portable coagulometer and who were reported their results to the Clinic, together with their suggestion of the appropriate dosage and of the date for the next attendance (Cosmi 2000). In reality, patients were asked to follow the dosage prescribed by the Clinic physician. The dosage suggested by the patients was compared to the one given to a control group followed at the Clinic with the traditional care. Dosage agreement was observed in 80% of the cases and the time spent within the therapeutic range was the same (80%) for self-testing patients and patients followed by the Clinic. This Italian study

further confirmed that OAT patients who are properly selected and trained to use portable coagulometers can autonomously measure their own PT INR with a positive advantage in convenience and possibly, although this has not been positively proven yet, with an improvement of clinical results.

### 1.2.2 Self-management

The concept of *self-management*, that is of total OAT self-management by the patient, appeared before portable coagulometers became commercially available. As a matter of fact, in 1974 Erdman evaluated 200 patients with prosthetic heart valves who were autonomously controlling their OAT using their physician's guidelines and the PT routinely measured by the laboratory (Erdman 1974). The percentage of patients with *therapeutic* anticoagulation was higher (98%) than that observed in a retrospective group of *usual care* patients (71%). Self-management became a particularly interesting model when portable instruments became available. Ansell *et al.* analyzed the results of self-management with one of these coagulometers in a cohort of 20 patients followed for 7 years, and compared these results with those in a control group of comparable age, sex and indication fro OAT who were followed by an AC (Ansell 1989, 1995). Self-managing patients had a PT within their therapeutic range in 88% of the cases whereas the PT of the control group was in therapeutic range 68% of the time ( $p < 0.001$ ), but there was no difference in the frequency of hemorrhagic and thrombotic complications.

Some studies compared *self-management* and *usual care* in both a prospective and randomized way. Horstkotte *et al.* studied 150 patients with prosthetic heart valves, observing that the 75 patients randomized to self-prescription were checking their PT INR every 4 days and had satisfactory anticoagulation in 92% of the cases, whereas the patients followed by their own physician were checked with the laboratory test every 19 days and had the PT INR within the therapeutic range in only 59% of the cases (Horstkotte 1996). Of particular interest was the observation that self-managing patients had a frequency of total hemorrhages and thromboses of 4.5% and 0.9% per year respectively, compared to 10.9% and 3.6% in the *usual care* group. Sawicki *et al.* randomized 90 patients to self-management, and compared them to 89 patients followed by their physician (Sawicki 1999). After 3 months of therapy, the *self-management* group had a significantly higher percentage of INR values within the therapeutic range than did the *usual care* group. Furthermore, in a large randomized study currently been carried out in Germany, of which only partial results are currently available (Koertke 2000), 305 *self-management* patients showed a higher frequency of PT INR

within range (78% vs 60%) and a lower prevalence of adverse effects (9.5% vs 15%,  $p=0.03$ ) than did 295 patients followed as *usual care*.

More recently, two controlled and randomized studies compared *self-management* to the *anticoagulation clinics* model of management. In a Dutch study with a *cross-over* design (Cromheecke 2000), 50 patients were randomized either to self-management or to be followed by a clinic for a period of 3 months; then each group switched to the other type of model for another 3-month period. The global quality of the two management systems was similar: patients remained within the therapeutic range 55% and 49% of the time spent in self-management and AC, respectively ( $p=0.06$ ). However, the patients' level of satisfaction was higher with self-management. In another German study (Watkze 2000), 49 self-management patients followed weekly were compared to 53 patients followed in an AC, where they were seen on average every 4-8 weeks. The self-management group had a higher percentage of checks within the range than did the AC group (84% vs 74%). Neither one of these two studies was, however, extensive enough to evaluate possible differences in the clinical complications of the different groups.

In conclusion, several studies have now established that OAT self-management is feasible and that in some cases it yields results that are better than *usual care* and at least similar to the ones of *anticoagulation clinics*. It must, however, be strongly stressed that these studies were carried out on a limited number of patients, who were highly selected from a very large number of anticoagulation patients. Furthermore, none of these studies has so far demonstrated a clinical advantage of *self-management* over *anticoagulation clinics*, that is over the current reference standard in OAT management. The (possible) improvement of the time spent within the therapeutic range, most likely due to the increased frequency of the checks, and the patients' greater satisfaction are interesting results achieved by *self-management*; these should, however, be regarded as surrogate *end-points* when compared to the real objective of OAT, that is the prevention of thromboses with the minimum risk of hemorrhage.

## 2. Portable coagulometers to determine INR

A new family of small, easy-to-use, portable coagulometers (monitors) based on dry-chemistry technology are now available. These monitors allow the determination of the INR also outside the laboratory (local hospital, community-based, general practitioners and patients), thus offering greater flexibility in managing anticoagulated patients.

### 2.1 How monitors work

Monitors consist of a small measuring unit and of a reactive strip (or cartridge) incorporating thromboplastin and calcium chloride in freeze-dried form. The sample to be tested consists of an unmeasured drop of capillary or venous blood without anticoagulant that is placed by the operators on the reactive part of the strip. The blood, carried inside the strip by capillarity, mixes with and rehydrates the thromboplastin, thus starting the coagulation reactions. The end-point recorded as a conventional prothrombin time (PT) is caused by the fibrin formation which stops blood flow within the capillaries, or by the thrombin generation which is quantitated by a specific probe. In other devices the thromboplastin preparation is mixed with iron particles that are kept in motion by a magnet. When the first fibrin strand is formed, the trapped iron particles stop moving and cause the timer to stop. Whatever the end-point, the PT is eventually converted into INR by means of the calibration parameters [international sensitivity index (ISI) and mean normal prothrombin time (MNPT)] encoded in the test strip.

### 2.2 Calibration of monitors

According to the *World Health Organization* (WHO), the calibration parameters (ISI and MNPT) needed to convert PT into INR must be determined through a process of calibration, which is detailed in the specific guidelines issued in 1999 (*WHO Expert Committee on Biological Standardization*, 1999). Although the above guidelines deal with the calibration of conventional INR measuring systems, they can be adapted also for the calibration of the monitors (Tripodi 1993, 1997, 2001). The calibration model proposed for the monitors in the early '90 (Tripodi 1993) has recently been subjected to a multicenter study sponsored by the European Union. This study confirmed the reliability and recommended the proposed model as the standard model to calibrate all monitors used for the laboratory control of patients on oral anticoagulants (Poller 2002). The responsibility of calibration rests entirely on the manufacturers, who should comply with the requirement and calibrate the devices according to the above recommendation.

### 2.3 Accuracy of INR measurement

Individual monitors (even though they have been calibrated) must be checked before release to the patient in order to assess their reliability. The assessment should be carried out by comparing the INR values on display with those obtained with a reference system. The reference system may be either an international standard for thromboplastin coupled with the manual technique to record coagulation time, or a system calibrated against one of the international standard for thrombo-

plastin (*WHO Expert Committee on Biological Standardization 1999, Tripodi 2001*). Although all monitors are designed and built to measure the INR and many of them are based on the same principle, generalization is not possible and their accuracy should be evaluated individually through specific studies (*Biasiolo 2000, Cosmi 2000a, Tripodi 2001*). At variance with the conventional INR measuring systems, the monitors bear the advantage of a simpler blood drawing, which makes testing possible also for unskilled operators such as the patient himself. However, this advantage may be obscured by the risk of increasing the variability in drawing capillary blood as opposed to venous blood. It is therefore mandatory to pay as much attention as possible in drawing capillary blood by finger stick (*Biasiolo 2000*) and to train the operator, especially if he/she is not a laboratory worker.

#### **2.4 Evaluation of the quality of results**

Reliability of INR measurement must be continuously checked through quality assurance programs that must include both internal and external (regional or national) schemes.

##### *2.4.1 Internal quality control scheme*

This can be carried out by the operator just before testing by using quality control materials at different levels of anticoagulation. These materials are usually supplied by the manufacturers and consist of freeze-dried samples. The user should test a drop of material (after proper preparation if required) on the test strip and compare the result on display with that specified by the manufacturer. In some monitors the above control can be preceded (or replaced) by an electronic control that checks all electronic functions of the monitor. The responsibility of the internal quality control scheme rests on the operator, who must be fully aware on the relevance of the scheme, on the way it must be carried out and on the action to be taken in case results are out of control. Before performing the measurement on blood sample, the operator must check whether the results of control samples are within the range of values supplied by the manufacturer. Results of internal quality controls should be entered in a file to allow for periodical statistical analysis. Further information to be recorded is the operator identity, the date and timing of testing, the lot numbers of the control materials and of the strips used for testing. The statistical analysis can be performed by the operator himself (if a laboratory worker, or general practitioner), or by the anticoagulant clinic if the operator is the patient or his/her own relative.

##### *2.4.2 External quality control scheme*

The purpose of this scheme is to assess periodically the performance of the monitor through the

analysis of unknown samples distributed by an external organizer, who is also independent from the manufacturer of the monitor. If the unknown samples are shared by many participants it is also possible to assess the relative performance of groups of monitors and estimate the agreement of the INR measurement among users that operate within the same country or region. To this end results obtained with individual monitors may be compared with the general (consensus) mean of all the participants in the same way as for the external quality assessment of conventional INR measurement. However, external quality assessment for the monitors represents a special case not yet fully addressed where the experience is still limited. Most monitors accept only non-citrated whole blood or plasma as testing material. Therefore, it would be impossible to supply all users with the same non-citrated sample. As an alternative, operators might be trained on how to reconstitute freeze-dried citrated plasmas with appropriate reconstitution fluids containing optimal amounts of calcium chloride. Calcium chloride would serve to antagonize the trisodium citrate used as anticoagulant, thus making testing possible even for citrated plasma. Although possible this system would not be applicable to all types of monitors as some of them accept only whole blood as testing material. While waiting for more appropriate solution, an acceptable (though demanding) alternative for the external quality assessment would be to recall periodically (two-three time/year) individual monitors and operators to the anticoagulant clinic where the INR for the same patients could be measured in parallel with the monitor and the laboratory reference system. Comparison of these paired values could be taken as the basis for assessing the monitor performance. Differences in excess of 20% should be regarded as unacceptable and the procedure repeated. If the difference persists the user should refer to the manufacturer for further investigation on the causes of failure.

### **3. Instructions to use portable coagulometers**

Portable coagulometers are the result of technological advances applied to the measurement of prothrombin time; they can potentially simplify and improve oral anticoagulation therapy in selected patients. A wide variety of these systems are commercially available. They allow the prothrombin time to be measured from a drop of capillary blood (similarly to how diabetic patients check their glycemia). Portable coagulometers are light, handy, easily transportable and, especially the newest ones, small. Determining prothrombin time requires a suitable drop of blood; this can be obtained by

picking a finger. The prothrombin time is expressed. Commercially available instruments use different technology to measure the clotting; the validity of these methodologies has been confirmed in the literature, which highlighted excellent correlation coefficients of the capillary and reference methods ( $r=0.96$ ) and a good analytical precision ( $CV=2.9-4.9\%$ ). These results are substantially the same for the various types of instruments.

In clinical practice, the development of portable instruments led to the appearance of *point of care testing*, transferring the analytical phase from the laboratory to the patient, with advantages in terms of convenience and practicality for the patient; the widespread use of portable instruments in some Northern European countries confirms this. As a matter of fact, portable coagulometers, which were initially developed to be used in health care settings by specialized personnel, are becoming commonly used for oral anticoagulation therapy self-testing and in some cases or countries, for *self-management*.

### **3.1 Training on portable coagulometer use**

Management safety of *self-testing*, and of *self-management* in particular, strictly depends on a number of critical steps. The patient must be capable of managing the instrument, of understanding its functioning and of using it properly.

The main purpose of training courses on portable coagulometers is to ensure *correct use* of the instrument and, for self-management courses proper OAT management. It is however necessary to remember that OAT monitoring is actually the simplification of a more complex activity.

*Patient Monitoring.* Several studies demonstrated that complications increase when the patient is not adequately informed on potential complications and when the checks are performed without suitable clinical evaluation. Proper training of the patient and knowledge about the system and the materials being used are therefore essential for correct use of the portable coagulometers. The patient must be supplied clear instruction manuals that, besides supplying the technical information on the instrument, include all the indications on how to carry out fingerstick puncture accurately and the list of all possible interferences. The user/patient must be taught how to use the analytical quality controls and how to behave when results are not acceptable.

Training courses are an important step in ensuring proper use of the instrument and therefore in ensuring greater OAT safety. However, to ensure good functioning of the system (instrumental and analytical control) and correct use by the patients (training courses and periodic re-evaluations), the widespread use of these systems should be subject to legislation and organizational regulation.

Potential users of portable coagulometers are:

- a) patients and/or their relatives
- b) health care personnel (physicians, nurses) both hospital-based and community-based.

The main objective of the training courses are to provide general information on OAT and the correct use of the portable coagulometer to determine prothrombin time (PT/INR). General training on anticoagulation therapy is of paramount importance to enhance more careful therapy management (Ansell J 2000).

Before giving an instrument to a patient or to an operator the following issues must be evaluated:

1. Physical handling skills of the operator.
2. Proper understanding of the way the test is to be carried out.
3. Verification of the actual capacity of obtaining correct results.

*A fundamental pre-requisite to the organization of training courses is the understanding that simply purchasing a portable coagulometer, although produced according to basic requirements and in compliance with European (CE) regulations, is not enough to guarantee the quality of the laboratory test (PT/INR) and the safety of the patient/user.*

### **3.2 General organization of the courses**

The proposed organizational model is based on indications and experience already validated in some European countries (Bernardo A 1996, Sawicki PT 1999), in which courses have been organized for several years for both self-determination of the prothrombin time (self-testing) and OAT self-management. We tried to determine a way of ensuring a *correct use* of these instruments, referring also to our direct experience (Cosmi B 1999, Cosmi B 2000). The users/patients who wish to participate in the courses should sign a request form that lists the details of the program. Different courses should be organized for PT self-testing and OAT self-management. Each course should have a maximum of 6 patients. It would be appropriate to set a national yearly calendar of the courses and to prepare educational material both on general oral anticoagulation therapy and specifically on the proper use of the portable coagulometer.

At the end of the course the patient should have a general understanding of blood coagulation and anticoagulation therapy and should be able to determine his or her PT-INR properly. Furthermore, the knowledge of the difficulties in obtaining the blood sample with a fingerstick is very important, because it is often lack of knowledge about this issue that causes unreliability of results (Biasiolo A. 2000).

### **3.3 Selection of the patients**

The selection of the patient (or of a relative) is of fundamental importance for therapy management.

Portable systems are recommended especially for the patients on long-term anticoagulation therapy. It is also thought to be safer to use portable coagulometers after the anticoagulation levels have become stable for at least 3 months within the therapeutic range, as this period is critical for possible complications. The physician in charge of the patient (FCSA Anticoagulation Clinic, general practitioner that has followed specific OAT training courses) can evaluate the clinical indications and patient's compliance. Poor compliance causes greater therapeutic instability (*van der Meer FJ 1997*) and this could be worsened by improper use of portable coagulometers.

In general, portable systems are recommended for:

- patients on stabilized oral anticoagulation therapy;
- patients who are to remain on OAT indefinitely or for the rest of their lives;
- *reliable* patients (or *reliable* relatives);
- patients restricted to their house or those who live in poorly accessible areas;
- patients with problematic venous access;
- patients with jobs that cause frequent or long absences.

Criteria for exclusion are a patient's unreliability or scarce compliance and previous thromboembolic and hemorrhagic complications. In the case of OAT self-management, the motivation to learn is fundamental for successfully completion of the training period. It is also been proposed that the patient's cognitive function is re-evaluated periodically, using standardized simple systems, such as the Mini Mental Test.

#### 4. Legislation and refundability

##### 4.1 Regulations on the use of monitors

Law #332 published in the *Gazzetta Ufficiale* dated September 8<sup>th</sup>, 2000 takes up the European Union Directive, 98/79/CE, on *in vitro* medico-diagnostic appliances. An *in vitro* medico-diagnostic device is defined as any device made of a reagent, a reactive product, a calibrating system, control material, a kit, an instrument, a device or a system, which is used by itself or in conjunction with something else, which its manufacturer designed for *in vitro* examination of human samples, including blood and donated tissues, with the single or main purpose of providing information on a physiological or pathological state, on a congenital abnormality or information that allows determination of the safety and compatibility with potential receiving subjects or the monitoring of therapeutic measures.

Monitors can be defined as *in vitro* medico-surgical appliances, although they are not formally included in the list of appliances.

The monitors *destination of use* is the "use to which the appliance is destined according to the information provided by the manufacturer on the label, instruction manual and in advertisements".

The fundamental requirements that the appliances should comply with are listed in Attachment I of the below listed legislative decree:

- "... their use (must) not compromise directly or indirectly the clinical condition or the safety of the patients ..."
- "... must provide the performance declared by the producer, especially in terms of analytical sensitivity and specificity, accuracy, repeatability ..."
- "... appliances for self-diagnostic tests must ensure that the appliance can be easily used by a layperson during all steps (of the test)"
- "minimize the risk of user's errors in using the appliance and in interpreting the results"
- "the instruction manual must include information on the sample to be used and on the possible special precautions to be taken to obtain such a sample"
- "the instruction manual must indicate if special training is necessary"
- "the instruction manual must indicate if the appliance is to be used together with other appliances"
- "the instruction manual must indicate the information on the type and frequency of the necessary maintenance and calibration operations"

Instructions must be specific for the appliances for self-diagnostic tests and must include a clear statement that the user must not take any decision of clinical nature without consulting his/her physician first. Furthermore, the instructions must indicate that the patient can adjust the treatment only if he or she has been trained accordingly.

The European Directive on regulating *in-vitro* medico-diagnostic appliances will become effective on December 7<sup>th</sup>, 2003. Monitors should therefore comply with the above basic law requirements, which are intended to ensure the INR quality obtained by the lay operator.

The above listed regulation could be properly applied in two phases: A) the first one, applied in other countries such as the U.S.A., evaluates the compliance of the self-diagnostic test systems to the use for which the system was manufactured; and B) the second one identifies the structures that can systematically comply with the procedures to correctly identify the systems, to train and provide information on their use and to monitor them.

The compliance evaluation procedures (basic requirements complying with the common technical specifications) can be carried out by the Health Ministry or by institutions that have been (previously) authorized after filing a request. In general,

the compliance evaluation does not take into account clinical data. The PT-INR measured by portable coagulometers does not require the efficiency conditions and standards normally used in evaluating the results of a clinical laboratory.

In order to obtain a positive compliance evaluation, it could be sufficient for the manufacturer to produce documentation of the type listed below:

- 150 patients enlisted in 6 centers for a 10 week study period;
- patients' selection based on pre-defined criteria;
- systematic instrument training period (*run in phase*);
- home delivery of the instrument, measurement and filing of PT-INR every week for 10 weeks;
- every two weeks the patient returns to the clinic or to his/her general practitioner and carries out the test with the instrument in front of the healthcare worker. The same health care figure then carries out the test on the patient with the same instrument and then draws venous blood to be tested in a certified laboratory to determine PT-INR;
- the agreement among the various measurements is then evaluated.

The Health Ministry or an authorized institution certifies the compliance of the instrument to the use for which it was built. The portable coagulometer can then become commercially available, but its use by the patient or by non-medical personnel requires the activation of phase B), in which specifically selected health-care workers prescribes a therapy plan.

#### 4.3 Therapy plan

As previously highlighted, the use of portable coagulometers by the patient requires: a) a critical evaluation of the patient's capability of carrying out the test; b) proper training on the correct way to use the instrument (and possibly training on self-prescription); c) the positive reliability of the result obtained with a specific instrument; d) monitoring the quality of results over time; e) monitoring the patient's physical and mental ability to obtain a correct result over time (and possibly monitoring his/her capability for self-prescription); f) the clinical re-evaluation of the patient. The responsibility for these procedures can be assigned to a specific clinic or, at least partially, to a general practitioner properly trained to monitor oral anticoagulation therapy.

The Anticoagulation Clinics constitute a network that covers the whole nation and are experienced in anticoagulation therapy and in training patients. The clinics are therefore the ideal centers to prescribe the therapy plan and to check the instru-

ments' quality periodically. The therapy plan could possibly include the request to the National Health System to refund the cost of the instrument and the diagnostic strips. As a matter of fact, in some clinical situations portable coagulometers appear to be necessary (difficult venous access, logistical impossibility of reaching laboratories or clinics), appropriate (patients who cannot walk and who are forced to stay at home) or recommended in terms of cost/benefit ratio (long term anticoagulation therapy, working age patients). This last aspect is not to be underestimated: the initial cost of the coagulometer (about 1,000 Euro, although the coagulometer can be re-used by several other patients) is counter-balanced by the reduction of other costs (loss of working hours for the patient and for relatives who have to accompany the patient, transportation costs) and by the reduction of work load for the clinic. The cost of the reactive strips and of the finger sticks (about 5 Euro) does not differ much from the cost of drawing venous blood in a clinic laboratory.

The following scenario can therefore be sketched: the portable coagulometer that has passed the compliance check by the Health Ministry can be purchased by the patient or can be assigned to him/her by the National Health System after a renewable therapy plan has been submitted. The therapy plan can be compiled by the physicians of approved structures (FCSA centers) or by general practitioners who have followed the specific courses jointly organized by the FCSA and the Italian Society of General Practitioners. The general practitioners who have compiled a therapy plan should, in any case, delegate the periodic checks of the instrument to a clinic, while awaiting a simplification of this procedure (see chapter 2).

#### 4.4 Refundability of portable coagulometers in other European countries

- Holland: mostly private (88%) health system, supported by religious or volunteer non-profit organizations. University hospitals are state run. Health insurance schemes are both private and public. Full refundability of the coagulometer, of the reactive strips, of the self-testing training course from April 2002. Anticoagulation clinics select self-monitoring patients (Dutch Government Gazette, 4 December 2001, N. 235, page 13).

- Germany: Public and private health insurance schemes. Full refundability of the coagulometer, of the reactive strips and of the training course.

- Denmark: Public health insurance. Full refundability of the coagulometer, of the reactive strips and of the training course since October 1999.

- Austria: Public health insurance. Full refundability of the coagulometer and of the reactive strips by several public insurance schemes (it varies from region to region).

- United Kingdom: Public health insurance. Refundability of the reactive strips only since May 2002.
- Spain: The health system is decentralized and regionally managed. Currently no refunds are available.

### Recommendations

The effectiveness of OAT and safety critically depend on the quality of therapy monitoring. The management of patients is recommended to be a continuous and systematic process that must include the review of laboratory tests and organized education, communication and follow-up system for the patients (recommendation level 1C) (see Appendix 1). Today, the management model that best meets these requirements is OAT Clinics.

OAT self-monitoring using portable coagulometers, both as self-testing and self-management, is a new therapy management model that has the potential advantage of being more convenient and of possibly improving the follow-up check quality, at least for some patients (recommendation level 2B) (see Appendix 1).

Strictly necessary self-monitoring requirements are: a) accurate selection and training of the patients; b) periodic checks of the measuring instrument by an independent institution; c) maintenance of an organized system for continuous training, communication and patients' follow-up. In any case, in order to satisfy these requirements it is recommended that the patients' self-management is followed and supervised by an Anticoagulation Clinic or by the patients' general practitioner.

In conclusion, based on current scientific knowledge, in order to ensure the safety of the patients

and the effectiveness of oral anticoagulation therapy, it is necessary to regulate the use of portable coagulometers in our country.

In particular, self-management appears to require the structuring of a monitoring system capable of checking the quality of OAT management over time and of systematically detecting complications, so that the cost-benefit ratio can be properly evaluated. It is necessary to establish a connection between the organization that implements the training program and the patient, who is to be properly followed although s/he has a greater autonomy.

A network of Anticoagulation Clinics (n=296) grouped in a Federation (FCSA) covers the whole Italian territory. These centers participate in training courses organized by the Federation. They can train patients and participate in compulsory check of therapy and laboratory quality. Using a therapy plan like the one outlined above, the clinics can identify patients who are suitable for using the portable coagulometers at home, they can organize training courses and they can distribute coagulometers, reactive strips, finger sticks

The dosage of anticoagulation can be adjusted by the clinic, by the general practitioner specifically trained for this purpose or by the patient himself/herself after a specific self-prescription course. The cost of all the above activities must be planned; it is therefore necessary to determine the maximum yearly number of patients who can benefit from portable coagulometers provided by the National Health System.

The same procedure can be applied to district points of district health care.

The clinics are responsible for the quality checks of the instruments.



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