INSTRUCTIONS FOR USE OF SIMPLE SIMON® PT

Product number ZAF 101-20MX Lot T032L MX Exp 2022-04

Updated July 16, 2018. Particularly important updates are in red and underlined.

IVD

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AREA OF USE

The IVD (in vitro diagnostic) product Simple Simon® PT (SSPT) is intended for determination of PT (prothrombin time), expressed in INR, in native blood, citrated blood and citrated blood plasma. The SSPT may be used for near-patient determination of PT(INR) at hospital laboratories, clinics and primary care centers. Simple Simon® PT is to be used by health care professionals with appropriate training. Appropriately trained operators will accomplish an analytical precision characterized by a CV <4%. SSPT is suited for monitoring the intensity of anticoagulant therapy with vitamin K antagonists such as the Waran® and Marevan®. Simple Simon® PT is an in vitro (ex vivo) diagnostic laboratory product. In performing a PT(INR) determination, the SSPT estimates the ambient room temperature, and the hematocrit (EVF) of the sample, see below. The estimates of temperature and EVF are used in the determination of PT(INR) and are not intended for other purposes. Simple Simon PT is intended for determination of PT(INR), not temperature nor EVF.

SUMMARY AND EXPLANATIONS

SSPT determines INR by a wet-chemistry procedure according to the methodology of Owren (ref 3). The liquid reagent contains, in addition to thromboplastin (membrane bound tissue factor), coagulation factor V and fibrinogen. The PT determinations, specific for the vitamin K dependent coagulation factors II, VII and X, are expressed in international normalized ratio, INR, the PT expression recommended by WHO. The INR is the ratio between sample PT and normal PT harmonized for best agreement to the WHO reference procedure. The harmonization is accomplished by powering the PT-ratio to the exponent ISI (International Sensitivity Index). Through innovative methodology (ref 4 & 5), samples of different kinds can be determined by the same analytical protocol (10 µL sample added to 200 µL reagent). The sample kinds that can be analyzed are native blood (capillary blood), citrated blood (venous blood) and citrated plasma. The EVF of the sample is estimated to distinguish blood form plasma, and also, for blood, the EVF estimate is used to compensate for the effects of out of the normal EVF-levels. The innovations also make it possible to perform the analysis at ambient room temperature in the range 17 to 40ºC (the reader needs not be thermostatted which greatly extends battery life, and there is no temperature equilibration during the analysis which saves time). Simple Simon® PT is calibrated to give INR values that agree with those generated by hospital laboratories calibrated with reference substance from EQUALIS, Uppsala. By this indirect route the SSPT is aligned with the WHO reference procedure.

GENERAL DESCRIPTION AND THE FUNCTIONS OF THE READER

In PT(INR) determination by Simple Simon® PT, one volume (10 uL) of sample is added to 20 volumes (200 uL) of reagent. The addition is by precise end-to-end capillary (MixxoCap®). When the sample is added to the reagent, the reagent is in a plastic reaction tube placed in the sample holder of the SSPT reader, where it is surrounded by light sources and sensors. Prior to the addition of sample the optical properties of the reagent are determined, and recorded. At the time of sample addition a timer is started. On the reader´s display, the operator is instructed to mix the sample and reagent. When the allowed time for the mixing (10 seconds) is up, the operator is instructed to remove the capillary. Five seconds later, the optical properties of the mixture, and the temperature, are determined and recorded. The two optical recordings, one of the reagent only, and one of the mixture, are used to estimate the EVF, and based on this EVF, the sample type, blood or plasma, is automatically decided. All through these described steps, ever since the addition of sample, the timer is running and will, together with information on sample type, temperature and EVF, and parameters stored in the reader, continuously calculate PT(INR) and show the value, in real time, on and reader's displayed. The displayed INR increases until the timer is stopped by the appearance of optical changes indicative of coagulation. If the sample is plasma there is no ambiguity, but if the sample is blood it is assumed to be capillary blood and the displayed INR is accordingly. If the blood is citrated (venous) blood (the reader cannot tell the difference, only the operator knows), the operator hits the single button of the reader, after the analysis is completed, and the INR of venous blood is displayed. For more information on how the SSPT reader determines INR by combining clotting time with information on temperature and EVF, see ref 4 & 5.

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The reader can detect certain irregularities in the analytical process including those of hardware, procedural errors, and analytical uncertainties, and if irregularities are detected, the reader will inform by messages on the display, and will then either refuse to operate, or to deliver potentially erroneous INR-results:
1. Autocheck: When the reader is powered up by a first hit on the button, information about the reader and the latest determination is displayed. A second hit on the button initiates an "autocheck". The reader checks battery voltage, shows this in symbols, and reminds if power shortage is close at hand. The reader also informs on number of additional tests that can be performed, see below under "Reader, Battery Replacement and Service Intervals". The reader also measures the temperature, and will perform analysis only if this is within the permissible range of 17 to 40°C, if not "low temperature" or "high temperature" is shown on the display. The reader then turns on the light source and if less light than expected reaches the light detectors the reader will display "weak light". There may be an obstruction in the lightpath which must be removed for the analysis to continue.
3. Mixing insufficiency: The reader will, by a motion sensors, detect the degree of mixing, and if this does not reach a preset level (80%), the reader will display "mix failed" and will not continue the analysis – the analysis must be redone.
4. Combat of disturbances: The reader will cope with disturbances that falsely give a clotting signal indicative of the beginning of clotting, but which have an insufficiently prominent aftermath, the search for the true clotting point then continues. Two such disturbances are allowed, but should there be a third, the reader will show "error", and the analysis is aborted.
5. Clotting errors: When a first optical sign of a clot is detected, the reader commences examination of the aftermath as mentioned in 4 above. If the aftermath signals are sufficiently prominent to permanently halt the analysis, a more extensive examination of the aftermath is performed. This aftermath examination is within a verification time zone of about 8 seconds. The examination requires two criteria to be fulfilled, if one or both is unfulfilled "error" is displayed, but no INR-results. One criteria is that a certain number of sufficiently large clotting signals are recorded inside the zone, the other is that the amount of transmitted light sufficiently deceases, drops, within the zone. A successful verification of the clotting is indicated by the message "clot OK, cup out". The operator then removes the reaction tube - and inspect its contents , see below - upon which the INR-result is automatically shown on the display.

THE REAGENT
Reagent for SSPT is delivered, portioned, in two flasks; one flask with a dry material, and one flask with buffer. All the buffer is used to dissolve/reconstitute all the dry material, and a PT reagent of the Owren kind is formed. The reagent contains optimal amounts of thromboplastin from rabbit brain, and of fibrinogen and coagulation factor V from bovine blood. The reagent also contains optimal amounts of free calcium ions, buffer substances and albumin. In the dry material there is a small amount of chromophore which turns yellow as it hydrolyzes. Because of this, the reagent will, slowly, over the course of days, turn increasingly yellow. This gives the operator an indication of how long the reagent has been reconstituted. Furthermore, should moisture leak into the flask of dry biochemicals, the "cake" will turn yellow. This indicates that the properties of the reagent may be compromised, and informs on the need of extra vigilance in checking the analytical performance by analysis of control plasma, such as ZAP. In preparing reagent, do not let the temperature of the flasks increase more than necessary before pouring the buffer into the reagent flask. Their temperature is 2 - 8°C when taken from refrigerated storage. For more details on handling the reagent, see Preparation below.

STABILITY AND STORAGE
The individually packaged product components are:
1. calibrated readers with pipette, 2. reagent, 3. control plasma, 4. reaction tubes, 5. stoppers, 6. pipette tips, and 7. bags of MixxoCap® .
The product components are delivered together as one product. All product components have the same lot number and the same expiry date. The expiry date is dictated by the least stable product component. None of the product components are to be used after the expiry date. All product components are to be stored according to the storage instructions on the individual packaging. The reagent, the control plasma (ZAP), and the ZAP BUFFER are stored refrigerated, 2-8°C. Other product components are stored at room temperature, 17-26ºC. For information on storage of reconstituted reagent and reconstituted control plasma, see "Preparation" below.

PREPARATION
1. **Dissolving (reconstituting) the freeze-dried (lyophilized) reagent**. Transfer/pour all of the contents of one flask of refrigerator cold (2-8°C) buffer into one flask of lyophilized biochemicals. Seal the reagent flask immediately with the screw cap of the buffer flask, and gently agitate the flask, and/or turn it repeatedly, upside-down. for at least 60 seconds until all dry material is dissolved. Mark the date on the label of the reagent flask. The reagent should be homogeneous and without visible, undissolved particles or lumps. The reagent is slightly opaque. Some of the opacity disappears shortly as it consists of small air bubbles released by the freeze-dried biochemicals. Some of opacity is permanent because it consists of hovering, micrometer large tromboplastin particles. If the reconstitution is performed in a temperature range of 15 to 20°C, an increase in opacity may be observed and the reagent will be slightly slower and give slightly higher INR values. When reconstitution temperature is >20°C, the described effects are more pronounced.
2. **Dispensing and storage of reconstituted reagent.** Arrange as many reaction tubes as needed in a rack, dispense 200 uL of dissolved reagent into each reaction tube, and stopper the tubes tightly with blue stoppers. If the tubes with reagent are to be used within five days, the rack with tubes may be stored, for a maximum of five days at room temperature (17-26°C). If the tubes with reagent are to be used within three weeks, the rack with tightly stoppered reaction tubes with reagent are stored, for a maximum of three weeks, refrigerated (2-8°C).

- **Details**; dispense the 200 uL of reagent into each reaction tube using the green pipette (200µL) supplied with the reader. The pipette is labeled with the lot number and the reader number. In starting the dispensing, attach (tightly!) a clean/"new" pipette tip to the green pipette. If other pipette is to be used, e.g. a repeater pipette, it is recommended to check that the other 200 uL pipette is OK by comparing PT results, i.e. INR-values, generated with reagent dispensed with the green pipette should agree with those generated with the reagent dispensed with the other pipette. A mean INR-difference of up to 0.05 INR-units may be accepted. After dispensing the reagent, the tubes are tightly sealed with clean/"new" blue stoppers (untight sealing will lead to evaporation during prolonged storage). It is important that the reagent is not contaminated during the dissolution or the dispensing, especially not with blood or blood plasma. The reagent is, of course, sensitive to coagulation factors and contamination of the reagent may, during the course of several hours to a day, affect the properties of the reagent. A high degree of contamination will lead to clot formation and make the reagent useless. Low degree of contamination may lead to less obvious changes in reagent properties. If the reagent, according analysis of control plasma, is OK one day after reconstitution, it is **not** contaminated.

3. **Reagent handling upon analysis.** Reaction tubes with reagent that have been stored refrigerated should be placed in the 18 position storage rack/magazine of the aluminum chassis of the reader and remain there for at least 15 minutes prior to use. Reaction tubes with reagent may then be stored, at room temperature, in the aluminum storage area/magazine of the reader, for five (5) days prior to use. Check periodically that accurate INR levels are generated by analysis of a control plasma.
4. **Reconstitution and handling of the control plasma ZAP** (Zafena Abnormal Plasma) is described in detail in the document included in the product, ZAF 102-1. In brief, the contents in one flask of ZAP is dissolved in 400 µl (2x200) cool, 10-15°C, blue ZAP BUFFER. The blue buffer is added (2x200 uL), using the green pipette supplied with the SSPT reader. Prior to pipetting, the blue buffer, stored refrigerated, is hand-warmed for about 30 seconds to raise its temperature somewhat. Pipetting cold buffer is not recommended, it will result in addition of less buffer than intended. Reconstituted ZAP can be used 10 minutes after the reconstitution. Stored refrigerated, reconstituted ZAP is stable for two weeks. Recommended storage is in the small plastic tubes provided, tightly capped. When reconstituted ZAP is taken from refrigerated storage, it should be hand-warmed for one minute, and it should also be homogenized (mixed). The homogenizing may be accomplished by moving a MixxoCap capillary around in the liquid. Avoid wetting the walls and stopper with ZAP liquid as this will increase evaporation and concentrate the plasma and reduces its INR-level.

WARNINGS AND PRECAUTIONS

Samples of blood and blood plasma may contain blood-borne infectious agents.
The samples can be contagious, and cause serious disease. Always use protection gloves when handling blood and blood plasma, including control plasma.

The reagent buffer, ZAF 101-2, and ZAP BUFFER, ZAF 102-2, contain sodium-azide to prevent bacterial growth.
The levels sodium azide, however, are low, less than 0.1%, less than 1 g/L, and formal warnings are not strictly necessary, yet it is informed that:
Azide is a quick acting poison which, like cyanide, blocks oxygen transportation in aerobic organisms, microbes as well as mammals.
- Do not drink, or otherwise take in, namned buffers and reagent and control plasma ZAP that reconstituted in these buffers.
- Flush with large amounts of water if the buffers, reagent or control plasma is poured down the drains, for drains made of metals there are special concerns.
- Do not pour above mentioned buffers or reconstituted reagents or plasmas down drains with tubing of lead or copper, azide reacts with named metals to form explosive compounds.

Material safety data sheet is provided on demand by the supplier or by Zafena AB.

THE READER, BATTERY REPLACEMENT AND SERVICE INTERVALS

The Simple Simon® PT reader is a battery-powered device that optically determines clotting time and hematocrit, and measures temperature. Using the measurements and stored calibration values the reader determines the INR of samples of plasma or blood, see above under "General Description of the Analytical Procedure and the Functions of the Reader", and ref 4 & 5.
The reader, after having its button hit a second, gives information, in symbolic form, of the condition of its batteries. Three big heart symbols indicate full battery. As the battery capacity decreases, the heart symbols become fewer and smaller. When only one small heart remains, the operator is reminded that a battery replacement is needed by having to execute an extra hit on the button to continue the analysis. When all hearts have disappeared the reader will not analyze, eventually the reader blacks out.
Battery replacement: The reader's three batteries, type AA, should be replaced when reminders on upcoming power shortage are given. Fresh batteries give the reader capacity to perform about 1200 analyses/tests. Instructions on battery replacement are found in the reader's packaging, and can be downloaded from ZAFENAs website, www.zafena.se .

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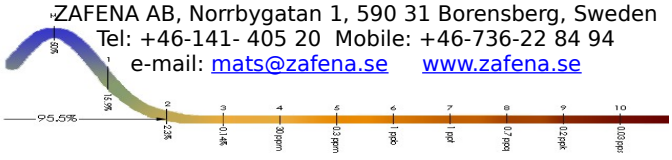


Power from outside source: Some readers, those with the text “USB & batteries”, can, via a USB connection, be powered from outside source. Battery consumption is then minimal and fresh batteries stay fresh for years. A USB-connected reader will operate without batteries, still it may be practical to have batteries also in USB-connected readers. Should the need arise to use the reader unconnected, or should there be a power failure, the batteries are automatically switched on to power the reader.
Service intervals: The reader is provided with an electronic test-counter, that informs on the number tests remaining before the reader must be serviced. For every test/analysis performed the number of remaining tests is reduced by one, and when zero is reached the reader requires service and will no longer function. Prior to this, a newly serviced reader should be ordered. The “old” reader can then be returned when the “new” reader is in operation. A newly serviced reader may typically display, "test remaining: 4000", for some users with MixxoCap this number has been increased to 6000. Even if the allowed number of tests have not been consumed, it is recommended that readers be used for a maximum of two years without service. In moving from one lot number of product to another, newly serviced readers, with the “new” lot number, will replace readers with the “old”. Readers that, for one reason or another, are taken out of service, should without delay be sent to the supplier or directly to Zafena AB, see www.zafena.no or www.zafena.se for shipping address. Readers taken out of service should not remain near the place of previous service because of the possibility that they again, mistakenly, be taken into service – this represents an analytical hazard.

PRODUCT COMPONENTS, STORAGE AND HANDLING
Simple Simon® PT, product no. ZAF 101, is composed of product components, these and their product numbers are: Calibrated reader, ZAF 101-1. Reagent, box(es) with flasks of lyophilized biochemicals, ZAF 101-2. Buffer, box(es) with flasks of liquid, ZAF 101-3. Green pipette, 200 µL, ZAF 101-5. Pipette tips, ~25 pieces suitable to green pipette, ZAF 101-6. Reaction tubes of clear polycarbonate, 400 pcs, ZAF 101-7. Stoppers to reaction tubes made of blue plastic, 400 pcs, ZAF 101-8. Instruction for use, ZAF 101-9. Bags of MixxoCap, 4x400 pcs, ZAF 103.
Receiving the product: Simple Simon® PT, product ZAF 101, are shipped in two packages. One contains the reader with the green pipette. The other contains consumables. The lyophilized reagent, ZAF 101-2, the buffer, ZAF 101-3, and the control plasma, ZAF 102-1, come in the same package as other consumables and should, shortly upon arrival, be separated and stored refrigerated (2-8°C).
Other product components are stored at room temperature (17-26°C), see storage instructions on the individual packaging of the product components.
Storage warning: Product components should not be stored in direct sunlight, and the product should not be used in direct sunlight.

PERMISSABLE OPERATING TEMPERATURE
Simple Simon® PT will determine PT(INR) at ambient room temperature in the range 17-40°C.

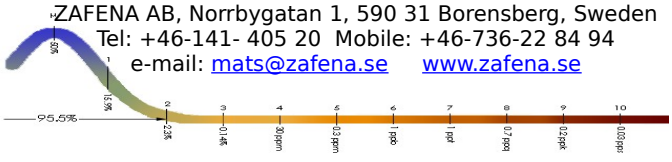
SAMPLE MATERIALS
The **S**imple Simon® PT performs PT(INR) analyses on 10µL of citrate anticoagulated plasma, citrate anticoagulated (venous) blood or native (capillary) blood.
CAUTION! Blood samples and plasma controls may carry infectious agents and cause serious disease. Always use gloves when sampling and analyzing.

INSTRUCTIONS FOR PERFORMING A PT(INR) ANALYSIS
Preparations, for a more information see above Under “the Reagent” and “Preparation”:

1. Reconstitute PT-reagent by pouring all the contents of one flask of buffer, ZAF 101-3, into one flask of freeze-dried reagent, ZAF 101-2.This is done immediately after the flasks come from refrigerated storage (temperature 2-8°C) . Seal the reagent flask with the screw cap of the buffer flask. Turn the reagent flask repeatedly upside down for at least 60 seconds, check that all dried material is completely dissolved, if not continue the agitation.
2. Dispensing and storage: The reagent is ready to use within 15 minutes from reconstitution and can be stored at room temperature for a maximum of 5 days dispensed in 200 uL portions in tightly stoppered reaction tubes.. If longer storage time is needed, tightly stoppered reaction tubes containing 200µL reagent are stored refrigerated. Dispensing is performed with the green pipette supplied with the reader and a yellow pipette tip, ZAF 101-6.
3. Handling refrigerated reagent: Place a suitable number of reaction tubes with reagent in the aluminum tube holder/magazine of the reader. Reaction tubes with reagent from the refrigerator can be “on the reader” for at least 15 minutes before use, and can stay “on the reader” for maximum of five (5) days prior to use.

Performing the PT(INR) analysis, the test:

1. Hit the button to power up the reader. The reader's display shows the latest test results, the lot number and number of remaining tests. Check that the lot number of the reader, the reagent and the other product components is the same.
2. Hit the button; reader performs an “autocheck”. If OK, the message “+200µL reagent” appears on the display. If not OK, other messages appear, see above under “.....Functions of the Reader”.
3. Place a reaction tube with reagent in the sample holder of the reader, secure the bayonet fitting, remove the stopper, replace the cover, and let the five second countdown reach zero. The reader checks for the presence of reagent (no reagent, no countdown). In moving the reaction tube, grip the tube by the stopper. Avoid touching the lower parts of the tube as not to disturb the temperature equilibrium. At the end of the 5 seconds countdown, “10 µL sample & mix” appears on the display. This message must appear, the analysis will otherwise not be performed. When “10 µL sample & mix” does appear, there is plenty of time for preparing the MixxoCap,



sampling and adding sample to reagent. After 10 minutes of operator inactivity the reader powers down to economize with the battery capacity.

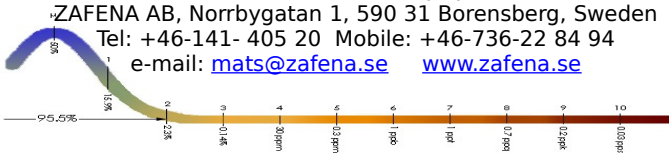
4. Prepare a MixxoCap; attach a blue mixxo-hat at the first position of the mixxo-body (check that the hat can be freely rotated, at the second position it can not).
5. Fill the capillary of the MixxoCap will sample. Bring the open end of the capillary in contact with sample, and allow sample to be drawn into the capillary by capillary force - this requires that the capillary is heavily slanted, held close to horizontally. Insure that the capillary is completely filled. If the blue mixxo-hat, by mistake, is in the second position the capillary will not fill.
6. Wipe the outside of the Mixxocap® capillary with a piece of adsorbing paper to remove excess of sample. Avoid contacting the capillary opening with the absorbing paper, sample can be sucked out of the capillary.
7. Add the sample to the reagent in the reaction tube in the reader's reaction tube holder. Place the open end of the capillary close to the surface of the reagent. With the ball of the thumb (not the tip of thumb's nail - wear gloves), forcefully depress the bellow of mixxo-hat so that mixxo-hat moves from first to the second position, and, simultaneously, lower the capillary opening towards the bottom of the reaction tube. Then, without delay, release, in a controlled manor, the pressure on the mixxo-hat bellow allowing it to expand and suck mixture of sample and reagent into the body of the MixxoCap. Sample has now been added to the reagent and the timer has been automatically started, the reader's display flashes “MIX!” and will do so for 10 seconds .
8. Mix sample and reagent by, in a controlled manor, alternately applying and releasing pressure on the bellow of the mixxo-hat. Never loose contact between thumb and mixxo-hat, depress and release (compress and expand) the bellow of the blue mixxo-hat. Movements in the mixture are registered by the reader during mixing, and are shown as percentage on the display. A minimum of movement (80%) must be registered during the 10 seconds of mixing. When ”pipette out” appears on the display, compress the mixxo-hat bellow a final time, hold it compressed, and remove the capillary. Four seconds later, “use cover” appears on the display.
9. Cover the opening of the sample holder of the reader with the aluminum lid that is fasten by a metal chain to the reader.
10. Wait for clotting to occur. PT(INR) analysis is complete when clotting has occurred, and the clot has been verified While the reader is on the look out for optical patterns indicative of clotting, the current INR-value is continuously updated and shown on the display. When the clotting patterns appear the updating is frozen and the aftermath is checked to verify the clot. During a time period of eight seconds, called the the verification zone, the “clotting signals”, symbolized by black bars, appear on the reader's display. During the verification the reaction tube must not be disturbed. At the end of the verification, either “clot OK” or “error” appear on the display. For more information on the clot detection, verification and “error”, see above under “General Description and Functions of the Reader”.
11. Remove the reaction tube from the holder of the reader when the “clot OK” and “cup out” alternately appear. The reaction tube is re-stoppered and the reaction tube removed, in that order. When the “cup” is removed the PT(INR) result appears. If sample is plasma (EVF<0.08), “plasma INR” is displayed. If sample is blood (EVF>0.08), the PT(INR) of native blood, “cap INR”, is displayed. If the blood is citrated blood (only the operator knows), the reader's button is hit and the result for citrated blood “ven INR” is displayed.
12. Inspect the contents of the reaction tube, the action may be called “reality check”. The “reality check” is to manually decide if clotting has occurred, or not. This is of special importance if reader shows “INR >8”, a non-clotted, fluid content is necessary, or the result is disqualified (repeat the analysis if a clot is found). The “reality check”, the inspection of the reaction tube content, is always of important as it increase analytical quality. As soon as the analysis is complete, i.e. when “cup out” is displayed, the reaction tube should be re-stoppered and lifted, turned upside down and inspected. A clot adhering to the bottom of the tube, alternatively an ongoing clot formation, is the required finding (except when the result is INR>8, see above). It is good, and recommended, operator practice to always inspect the contents of the reaction tube immediately upon completion of analysis. Unexpected findings of any kind prompts the operator to repeat the analysis.
13. Hit the button repeatedly and various information on the analysis is displayed in succession, repeatedly; EVF, clotting time and temperature Only the INR-value is intended for medical diagnostic purposes, the other pieces of information are of possible value to the operator. Information on time, temperature and EVF are **not** for diagnostic use.
14. Inactivate the reader by holding the button down for two (2) seconds. Inactivation of reader can be performed at any stage of analysis. Inactivation is necessary before starting a new analysis. To minimize power consumption, the reader will automatically inactivate itself, power down, if no operator activity is recorded within ten (10) minutes.
15. Make an assessment of if the test result is reasonable. If result is unexpected, low or high or otherwise atypical, the operator should repeat the analysis to increase the analytical quality. Results of duplicate analysis that differ by more than 20% should not be accepted.

LIMITATIONS

It is not possible to perform PT analyses outside of the temperature range 17-40°C. Do not use, or place, the SSPT equipment direct sunlight.

Lupus anticoagulant has little or no effect on PT(INR) determinations by SSPT, as by other other PT(INR) determination by methodology according to Owren (ref 3)

Therapeutic levels of heparin in the samples typically do not impact on the PT(INR) determination by SSPT. Unfractionated heparin at plasma levels of 1 IU/mL will elevate the PT(INR) results by by about 10%, the effects of fractionated heparin is



less pronounced. High levels of heparin in the sample will give erroneously high INR-values. Higher levels of NOAC will elevate the results of SSPT, therapeutic levels typically have negligible effect. Experiments with normal plasma spiked with NOAC indicate that 10% elevation of the INR-results occur at:

dabigatran	>100 ug/L
apixaban	>125 ug/L
rivaroxaban	>60 ug/L

INTERPRETATION OF RESULTS

PT results, according to WHO recommendations, are expressed in INR, International Normalized Ratio, PT(INR) or just INR, see ref 1 and above under "Summary and Explanations". PT(INR) results less than 0.7 are very rare, perhaps non-existent, and SSPT will not display INR below 0.7. The highest INR that the SSPT will display is INR 8.0, which upon request can be raised to INR 10.0.

Normal health individuals show an average INR of 1.00.

Unless otherwise prescribed by physician, the intensity of treatment with vitamin K antagonists is adjusted to give an INR in the range 2.0 to 3.0.

Elevated INR-values above a limit, set by local medical expertise, require immediate attention of physician. This limit can differ from one health care organizations to another, but is typically in the range INR 6.0 to 8.0.

REFERENCE VALUES

Expected values.

Normal range;

INR 0.92-1.20 (corresponds to PK-activity between 130% and 70%), ref 3.

Therapeutic range in thrombosis prophylaxis;

INR 2.0-3.0 (corresponds to PK-activity between 25% and 15%), ref 3.

MEASURING RANGE

Simple Simon® PT measures prothrombin time in the range INR 0.7 to INR 8.0. The measuring range, if desired, can be extended to INR 0.7 to INR 10.0 .

PRECISION

In well trained operators' hands, **S**imple Simon® PT determines PT(INR) with a precision comparable to those of methods used at Nordic hospital central laboratories, within-series CV<2.5% in the range INR 2 to INR 3.

STANDARDIZATION

The SSPT is calibrated with authentic samples from normal individuals and patients on vitamin K antagonists. The samples have a known INR-values by analysis performed at a Nordic hospital central laboratory by an Owren PT method calibrated with calibrator substances from EQUALIS, Uppsala, according to "Certificate of analysis of calibrators and control materials intended for PT analysis (INR) according to Owren" (EQUALIS Version 2.0, see ref 3. These INR-levels are ensured to agree with the international reference procedures, ref 3, and thus, indirectly, ensure that INR-values by SSPT agree with the international reference procedures, particularly the one based on the International Reference Preparation RBT/05. Several users of SSPT check the INR-levels regularly by analysing citrated (venous) blood in primary care settings, and then submitting the sample to hospital central laboratory for comparative PT(INR) analysis according Owren.

CONTROL MATERIALS

Control material for checking the performance of **S**imple Simon® PT may be most any commercially available lyophilized, coagulation control plasma, or pooled plasmas stored frozen in portions.

Zafena recommends the use of Zafena Abnormal Plasma, ZAP, which is included in the product. When analyzed by SSPT, ZAP shows an average INR-values close to the middle of the therapeutic range.

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