Summary of safety and performance – IN

This Summary of Safety and Performance (SSP) is intended to provide public access to an updated summary of the main aspects of the safety and performance of the device.

The SSP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients. The following information is intended for users/healthcare professionals.

1. Device identification and general information

1.1. Device trade name

IN (REF 1031EU)

1.2. Manufacturer

APIRO Diagnostics Kft.

Liget utca 3/2, HU-2040 Budaörs, Hungary

1.3. Manufacturer's single registration number (SRN)

HU-MF-000043501

1.4. Basic UDI-DI

59998629921031EU_1TV

1.5. European Medical Device Nomenclature (EMDN)

W01030299 - Haemostasis reagents – other

1.6. Risk class of device

Class C. Classification rules 3j and 3k

1.7. Year when the device was first CE-marked under Regulation (EU) 2017/746 covering the device

2026

1.8. Authorized representative

n/a

1.9. Notified Body

3EC International a.s. (2265)

2. Intended purpose and other indications

2.1. Intended purpose

The IN is a ready to use reagent for in-vitro diagnostic professional use, intended for detection of unfractionated heparin in citrated blood during viscoelastometry analysis.

2.2. Indication(s) and target population(s)

Indicated to be used when the presence of unfractionated heparin in the adult patient's blood is suspected.

2.3. Indication whether it is a device for near-patient testing and/or a companion diagnostic

The IN assay is not intended for near-patient testing.

The IN assay is not intended for a companion diagnostics.

2.4. Limitations and/or contra-indications

The assay shall not be used in patients treated with DOACs, as this can lead to false-positive results in the IN assay.

The mechanism of the IN assay is not specific to unfractionated heparin. Other anticoagulants such as direct factor Xa inhibitors or thrombin antagonists can also prolong clotting times and lead to false-positive results in the IN assay. Factor deficiencies can prolong the clotting times and lead to false-positive results.

3. Device description

3.1. Description of the device

The IN assay is a dry chemistry reagent for the assessment of coagulation activation in whole blood, triggered using ellagic acid (coagulation activator via the intrinsic pathway). It also contains calcium chloride for the recalcification of the citrated blood sample, a pipette tip and a reagent carrier. Intended for laboratory use.

3.2. Description of the components

The sales unit of the device contains 10 individually sealed single-use pouches containing one pipet tip with reagent each, providing a dry chemistry reagent composed of ellagic acid and calcium

chloride. Each pouch contains one desiccant bag. Each individually sealed tip is used for one analysis, i.e. the sales unit of the device allows to perform 10 tests.

3.3. Previous generations or variants of the device

The current device generation is the first, thus there are no previous generations of the device.

3.4. Description of any accessories which are intended to be used in combination with the device

No accessories required.

3.5. Description of any other devices and products which are intended to be used in combination with the device

Device name	Device REF	Device type	Device manufacturer
MultiClot	3011EU	analyzer	APIRO Diagnostics Kft.
Cups & Pins	4011EU	receptacles	APIRO Diagnostics Kft.
QC1	2011EU	positive control	APIRO Diagnostics Kft.
QC2	2021EU	negative control	APIRO Diagnostics Kft.
ClotPro 6.0	111010	analyzer	enicor GmbH
Cups & Pins	112010	receptacles	enicor GmbH
QC1	113101	positive control	enicor GmbH
QC2	113102	negative control	enicor GmbH

4. Harmonised standards and CS applied

Following harmonized standards were applied during the development and lifecycle of the device:

EN ISO 13485:2016 + A11:2021 *Medical devices — Quality management systems — Requirements for regulatory purposes*

EN ISO 14971:2019 + A11:2021 *Medical devices — Application of risk management to medical devices*

EN ISO 15223-1:2021 *Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements*

Common specifications as defined in the IVDR have not been developed to date for the device.

5. Risks and warnings

5.1. Residual risks and undesirable effects

The following residual risks were identified during the risk management activities for the device:

- In case of an off-label use of the product, test results may be incorrectly interpreted by the user.
- In case of device handling errors, patient's coagulation may be incorrectly reflected.
- In case of the use of the expired product, patient's coagulation may be incorrectly reflected.
- In case of unacceptable transport and storage conditions, patient's coagulation may be incorrectly reflected.

No undesirable side-effects were identified during the post-market activities for the device.

5.2. Warnings and precautions

CAUTION: A use of the device outside of its intended purpose, may lead to the test results being incorrectly interpreted by the user.

CAUTION: Incorrect storage conditions may affect reagent stability and lead to wrong test results.

CAUTION: Do not use tips from defective pouches or from pouches missing the desiccant pack.

CAUTION: Intended for single use - do not reuse.

CAUTION: Any serious incident that has occurred as a result of the use of the device has to be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established.

CAUTION: Failure to comply with these instructions for use may result in device handling errors leading to wrong test results.

CAUTION: Human blood samples should be handled with care, following general precautions recommended for bio-hazardous materials.

CAUTION: General precautions (e.g., wear gloves and minimize skin exposure to specimens and reagents) should be followed when handling all materials.

NOTE: Dispose of waste according to local regulations.

NOTE: A material safety data sheet is available upon request.

CAUTION: Collect a venous blood sample according to the recommended procedures using a blood collection tube with 3.2% sodium citrate. Samples should be analyzed within 3 hours from blood collection. Store the blood at room temperature. Always ensure blood collection tubes are filled to the indicated fill volume to avoid excessive citrate levels.

CAUTION: Do not use the expired product. The use of the expired product may lead to wrong test results.

5.3. Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN)

No FSCA or FSN were issued for the device to date.

6. Summary of performance evaluation and post-market performance follow-up (PMPF)

6.1. Summary of scientific validity of the device

The IN assay is a functional whole-blood based assay to be used on viscoelastometry analyzers (Volod 2022) which uses the contact activator ellagic acid for the activation of the intrinsic pathway of blood coagulation. Viscoelastometry is widely used worldwide and its applications have been summarized for example in Volod 2022.

Volod O, Bunch CM, Zackariya N, Moore EE, Moore HB, Kwaan HC, Neal MD, Al-Fadhl MD, Patel SS, Wiarda G, Al-Fadhl HD, McCoy ML, Thomas AV, Thomas SG, Gillespie L, Khan RZ, Zamlut M, Kamphues P, Fries D, Walsh MM. Viscoelastic Hemostatic Assays: A Primer on Legacy and New Generation Devices. J Clin Med. 2022 Feb 7;11(3):860.

The detection of unfractionated heparin using functional coagulation assays, triggered via the contact pathway is common practice. Such assays are the aPTT (activated partial thromboplastin time) (McLaughlin 2019), the ACT (activated clotting time) (McLaughlin 2019), or viscoelastometry-based tests such as the in-tem®, IN-test or the IN assay (Heubner 2022). Due to their mode of action such assays are sensitive for unfractionated heparin but provide a relatively modest correlation of the clotting time / aPTT / ACT vs. the anticoagulant concentration as determined using chromogenic substrate-based assays (such as the anti-Xa test) (McLaughlin 2019, Falter 2020).

McLaughlin K, Rimsans J, Sylvester KW, Fanikos J, Dorfman DM, Senna P, Connors JM, Goldhaber SZ. Evaluation of Antifactor-Xa Heparin Assay and Activated Partial Thromboplastin Time Values in Patients on Therapeutic Continuous Infusion Unfractionated Heparin Therapy. Clin Appl Thromb Hemost. 2019 Jan-Dec;25:1076029619876030.

Falter F, MacDonald S, Matthews C, Kemna E, Cañameres J, Besser M. Evaluation of Point-of-Care ACT Coagulometers and Anti-Xa Activity During Cardiopulmonary Bypass. J Cardiothorac Vasc Anesth. 2020 Nov;34(11):2921-2927.

Heubner L, Mirus M, Vicent O, Güldner A, Tiebel O, Beyer-Westendorf J, Fries D, Spieth PM. Point of care coagulation management in anesthesiology and critical care. Minerva Anestesiol. 2022 Jul-Aug;88(7-8):615-628.

Two studies report significant correlations of the INTEM CT values with the anti-Xa test in patients treated with unfractionated heparin (Schultinge 2023, Yin 2025).

Schultinge L, Hulshof AM, van Neerven D, Mulder MMG, Sels JEM, Hulsewe HPMG, Kuiper GJAJM, Olie RH, Ten Cate H, van der Horst ICC, van Bussel BCT, Henskens YMC. Applications of rotational thromboelastometry in heparin monitoring in critical COVID-19 disease: Observations in the Maastricht Intensive Care COVID cohort. Thromb Update. 2023 Aug;12:100140.

Yin EB, Bracey AW, Chatterjee S. Thromboelastography versus thromboelastometry for unfractionated heparin monitoring in adult patients on extracorporeal membrane oxygenation. Perfusion. 2025 Jan;40(1):235-242.

6.2. Summary of performance data from the equivalent device

Yin et al (Yin 2025) report an R value (Spearman) of 0.624 (p=0.003) for the INTEM CT vs Anti-Xa in a cohort of adult patients on ECMO (N=20).

Schultinge et al (Schultinge 2023) report an R value (Spearman) of -0.531 (p=0.034) for the INTEM CT vs. Anti-Xa in a cohort of COVID-19 patients treated with UFH (N=16).

INTEM CT precision data is provided in the 510k of the widely used ROTEM sigma device. In K201440 the results of the 510k evaluations for the ROTEM sigma device are summarized.

https://www.accessdata.fda.gov/cdrh_docs/pdf20/k201440.pdf

For the INTEM CT within-laboratory precision CV values of 3.8% - 6.8% are reported.

6.3. Summary of performance data from conducted studies of the device prior to CE-marking

In a precision study citrated blood with and without the addition of 0.5 anti-Xa U/mL unfractionated heparin was tested in 3 runs, on three analyzers, three operations and including 3 IN assay lots (54 determinations per sample). The resulting mean, standard deviation (SD) and coefficient of variation (CV) for the CT were as follows:

	mean	SD	CV
citrated blood (CB)	158.2	4.7	3.0%
citrated blood (CB) + 0.5 IU/mL UFH	269.6	20.9	7.8%

To assess the sensitivity and specificity for the IN assay for the detection of heparin, a cut-off of 0.3 U UFH / mL was applied, which represents the lower level of the therapeutic range.

When a patient group treated with UFH (n=101) and a control group (control subjects, n=103) are analyzed together using a cut-off of 190 sec for the IN-test CT, the sensitivity, specificity, positive predictive value and negative predictive values were as follows:

Sensitivity	94%
Specificity	97%
Positive predictive value (PPV)	91%
Negative predictive value (NPV)	98%
Positive likelihood ratio	28.3
Negative likelihood ratio	0.06

The reference range for the IN assay clotting time (CT) was determined in a clinical study including 123 healthy individuals, aged 18.9 - 79.2 years, 51.2% female and 48.8% male, by the calculation of the 95% central interval (2.5° percentile – 97.5° percentile). The resulting reference range is 113-164 sec.

6.4. Summary of performance data from other sources

There is no data of performance from other sources.

6.5. An overall summary of performance and safety

The performance evaluation, including scientific validity, analytical performance, and clinical performance studies, has been conducted in accordance with the requirements of Annex XIII of the Regulation (EU) 2017/746 (IVDR). The evaluation confirms that the device meets the applicable GSPR as set out in Annex I of the IVDR.

The device demonstrates:

- Scientific validity for the intended analyte and clinical condition, supported by relevant scientific literature and established clinical practice;
- Analytical performance, including precision, specificity, sensitivity, linearity, and robustness, all validated through structured and statistically sound studies;
- Clinical performance, confirmed through clinical studies showing strong concordance with standard reference methods and demonstrating the clinical utility of the related products in their intended context.

Furthermore, all known and foreseeable risks have been systematically assessed and addressed through risk management and performance evaluation processes. The residual risks are mitigated to an acceptable level in accordance with the state of the art, and appropriate risk control measures are in place and communicated effectively to the user.

6.6. Ongoing or planned post-market performance follow-up

Post-market performance follow-up are planned to be performed every year.

7. Metrological traceability of assigned values

7.1. Explanation of the unit of measurement

Viscoelastometry is a functional method that continuously measures coagulation in whole blood, by detecting the elasticity (mechanical quality) of the blood clot during the coagulation process (Volod 2022). For historical reasons the blood clot firmness is expressed in millimeters (mm). The clotting time is the time from the start of the test until an amplitude of 2 mm is detected. It is expressed in sec. The clot firmness is quantified by the amplitude 5 min after CT (A5), amplitude 10 min after CT (A10), amplitude 20 min after CT (A20) and the maximum clot firmness (MCF). The clot stability or fibrinolysis is quantified by the maximum lysis parameter (in %).

Volod O, Bunch CM, Zackariya N, Moore EE, Moore HB, Kwaan HC, Neal MD, Al-Fadhl MD, Patel SS, Wiarda G, Al-Fadhl HD, McCoy ML, Thomas AV, Thomas SG, Gillespie L, Khan RZ, Zamlut M, Kamphues P, Fries D, Walsh MM. Viscoelastic Hemostatic Assays: A Primer on Legacy and New Generation Devices. J Clin Med. 2022 Feb 7;11(3):860.

7.2. Identification of applied reference materials and/or reference measurement procedures of higher order used by the manufacturer for the calibration of the device

For viscoelastometry as a functional whole blood method no international reference material or SI unit exists. In the clinical study the UFH concentration was determined with the anti-Xa method on the CoagXL analyzer (Diagon, Budapest, Hungary). This method was calibrated using a reference material which was calibrated against the international standard for unfractionated heparin.

8. Suggested profile and training for users

The device is intended to be used by:

- trained healthcare professionals
- trained laboratory professionals

The users are trained using standard strategies by trained personnel e.g. field service representatives of the local distributor. The training is performed using the instructions for use, and the viscoelastometry device and its documentation owned by the user.

9. Revision history

SSP revision number	Date issued	Change description	Revision validated by the Notified Body
1	2025-12-15	Initial version	☒ yes – validation language: English ☐ no
2	2026-07-28	Addition of compatible devices in Section 3.5. Correction of the year in Section 1.7	☐ yes ☒ no