

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k120977

B. Purpose for Submission:

To obtain clearance of control material for the ACT+ and ACT-LR assays using HEMOCHRON Microcoagulation Systems

C. Measurand:

Activated Clotting Time (ACT)

D. Type of Test:

Quantitative clotting assay

E. Applicant:

International Technidyne Corporation

F. Proprietary and Established Names:

*direct*CHECK® Controls for HEMOCHRON® Microcoagulation System ACT+
cuvette

*direct*CHECK® Controls for HEMOCHRON® Microcoagulation System ACT-LR
cuvette

G. Regulatory Information:

1. Regulation section:
21 CFR§ 864.5425, Multipurpose system for in vitro coagulation studies
2. Classification:
Class II
3. Product code:
GGN, Plasma, Coagulation Control
4. Panel:
Hematology (81)

H. Intended Use:

1. Intended use(s):

The directCHECK® Whole Blood ACT+ Level 1 (normal) and ACT + Level 2 (abnormal) Controls are assayed lyophilized whole blood preparations intended for the quality control of quantitative coagulation test: HEMOCHRON® ACT+ assay cuvette on the HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite instruments.

The directCHECK® Whole Blood ACT-LR Level 1 (normal) and ACT-LR Level 2 (abnormal) Controls are assayed lyophilized whole blood preparations intended for the quality control of quantitative coagulation test: HEMOCHRON® ACT-LR assay cuvette on the HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite instruments.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For Prescription Use Only

4. Special instrument requirements:

For use only with the Hemochron® Jr. Signature+ and Hemochron® Signature Elite Instruments.

I. Device Description:

The *direct*CHECK® ACT+ Level 1 and Level 2 are whole blood assayed quality controls reagents that are lyophilized whole blood preparations made from animal plasma fixed with animal red blood cells for one time single use. The whole blood preparations are lyophilized into 1 mL individual glass ampoules with an internal separate liquid diluent. When the glass ampoule is broken, the diluent rehydrates the lyophilized material, forming a liquid whole blood control.

The *direct*CHECK® ACT-LR Level 1 and Level 2 are whole blood assayed quality controls that are lyophilized whole blood preparations made from animal plasma fixed with animal red blood cells for a one time single use. The whole blood preparations are lyophilized into individual 1 mL glass ampoules with an internal separate liquid diluent. When the glass ampoule is broken, the diluent rehydrates the lyophilized material, forming a liquid whole blood control.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Hemochron® Jr. Microcoagulation ACT-Long Range Whole Blood Controls
Hemochron® Jr. Microcoagulation ACT+ Whole Blood Controls

2. Predicate 510(k) number(s):

k960749

k941007

3. Comparison with predicate:

| Similarities | | |
|----------------------|---|--|
| Item | Device <i>direct</i> CHECK® ACT+ Whole Blood Level 1 & 2 Controls (k120977) | Predicate Hemochron® ACT+ QC Level 1 & 2 (k941007) |
| Intended Use | The <i>direct</i> CHECK® Whole Blood ACT+ Level 1 (normal) and ACT + Level 2 (abnormal) Controls are assayed lyophilized whole blood preparations intended for the quality control of quantitative coagulation test: HEMOCHRON® ACT+ assay cuvette on the HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite instruments. | The ACT+ Quality Control Product is a lyophilized whole blood preparation that is used to perform a quality control assay using the HEMOCHRON® Jr. Microcoagulation ACT+ test cuvette. |
| Material Composition | Non-human plasma, non-human red blood cells and diluent (containing calcium chloride) | Non-human plasma, non-human red blood cells and diluent (containing calcium chloride) |
| Analyte | ACT+ | ACT+ |
| Test System | HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite instrument. | Same |

| Differences | | |
|---------------------|---|---|
| Item | Device <i>direct</i> CHECK® ACT+ Whole Blood Level 1 & 2 Controls (k120977) | Predicate Hemochron® ACT+ QC Level 1 & 2 (k941007) |
| Form | Ready to use squeezable dropper containing liquid diluent and glass ampoule which contains lyophilized pellet | Three vials: lyophilized control, diluent, and calcium chloride |
| Storage | 2 to 8°C | 4 to 8°C non-punctured vials |
| Open vial stability | Single-use, disposable, use immediately | May be kept at room temperature for a maximum of one hour. |

| Similarities | | |
|----------------------|--|---|
| Item | Device <i>direct</i> CHECK® ACT-LR Whole Blood Level 1 & 2 Controls (k1210977) | Predicate Hemochron® ACT-LR QC Level 1 & 2 (k960749) |
| Intended Use | The <i>direct</i> CHECK® Whole Blood ACT-LR Level 1 (normal) and ACT-LR Level 2 (abnormal) Controls are assayed lyophilized whole blood preparations intended for the quality control of quantitative coagulation test: HEMOCHRON® ACT-LR assay cuvette on the HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite instruments. | The HEMOCHRON® Jr. Microcoagulation Whole Blood Controls are lyophilized whole blood preparations which have been assayed and are intended to be used to perform quality control assays using the HEMOCHRON® Jr. Microcoagulation ACT-LR test cuvettes. |
| Material Composition | Non-human plasma, non-human red blood cells and diluent (containing calcium chloride) | Same |
| Analyte Tested | ACT+ | Same |
| Test System | HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite instrument | Same |

| Differences | | |
|--------------------|---|---|
| Item | Device <i>direct</i> CHECK® ACT-LR Whole Blood Level 1 & 2 Controls | Predicate Hemochron® ACT-LR QC Level 1 & 2 (k960749) |
| Form | Ready to use squeezable dropper containing liquid diluent and glass ampoule which contains lyophilized pellet | Three vials: lyophilized control, diluent, and calcium chloride |
| Storage | 2 to 8°C | 4 to 8°C non-punctured vials |
| Open Vial Claim | N/A, single-use, disposable, use immediately | May be kept at room temperature for a maximum of 1 hour |

K. Standard/Guidance Document Referenced (if applicable):

- CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods, 2nd Edition
- CLSI EP17-A: Protocols for the Limit of Detection and Limit of Quantitation; Approved Guideline
- CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents: Approved Guideline
- FDA Use of Symbols on Labels and in Labeling of In-vitro Diagnostic Devices Intended for Professional Use

L. Test Principle:

The *directCheck*® Whole Blood Quality Controls are dried whole blood preparations which have been assayed and are intended to be used to perform quality control on the ACT+ and ACT-LR test cuvettes on both the HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite analyzers. The analyzers utilize the end point clot detection with the addition of an activator (celite) to initiate the intrinsic pathway. Once a clot end-point is detected, the clotting time is displayed.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within-site repeatability was determined for 3 lots of each control level for the ACT+ and ACT-LR controls. For each lot of control 20 replicates were tested in duplicate on each instrument (HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite analyzers) for one day. The %CV for each lot/instrumentation combination meets the pre-specified acceptance criteria of CV<14.0%.

Please see the table below for a summary of results.

| Controls | n | mean | Within-run SD | Within-run %CV |
|----------------|-----|------|---------------|----------------|
| ACT-LR Level 1 | 120 | 128 | 13.2 | 9.2% |
| ACT-LR Level 2 | 120 | 239 | 23.1 | 9.7% |
| ACT+ Level 1 | 120 | 154 | 11.0 | 7.1% |
| ACT+ Level 2 | 120 | 402 | 7.7 | 1.9% |

Reproducibility was assessed in two reproducibility studies (inclusive of a revised study) conducted on three lots of controls according to CLSI EP5-A2 guidelines.

Testing was performed twice daily in duplicate over 20 consecutive days using two separate instruments at three sites with 2-3 operators per site. The initial reproducibility study used only one lot of control, and the revised study incorporated two additional control lots. Pooled data from the combined studies tested on the HEMOCHRON® Jr. Signature+ and HEMOCHRON® Signature Elite was assessed. The %CV and SD for within-run, between-run, between-lot, between-site, between site and total precision was determined for ACT+ and ACT-LR. Results met the pre-determined overall acceptance criteria of %CV ≤ 12.0 for ACT+ and %CV ≤ 14.0% for ACT-LR as summarized in the table below:

| Sample | n | Mean | Within-Run (SD, %CV) | Between-Run (SD, %CV) | Between-Day (SD, %CV) | Between-Site (SD, %CV) | Between-lot (SD, %CV) | Between instrument (SD, %CV) | Total (SD, %CV) |
|----------------|-----|------|-------------------------|--------------------------|--------------------------|---------------------------|--------------------------|---------------------------------|--------------------|
| ACT-LR Level 1 | 240 | 122s | 12.1 9.8% | 8.6 7.40% | 4.0 3.4% | 4.5 3.8% | 18.2 15.7%* | 5.7 4.78% | 17.2 14.0% |
| ACT-LR Level 2 | 240 | 250s | 19.0 7.2% | 15.6 7.1% | 5.6 2.0% | 4.8 3.1% | 55.7 22.3%* | 7.6 3.1% | 26.4 10.1% |
| ACT+ Level 1 | 240 | 154s | 9.9 6.4% | 5.1 3.4% | 3.1 2.0% | 4.5 3.0% | 3.3 2.2% | 1.9 1.0% | 12.5 8.2% |
| ACT+ Level 2 | 240 | 405s | 9.0 2.2% | 4.3% 1.1% | 1.5 0.5% | 2.8 0.5% | 9.6 2.4% | 1.0 0.4% | 10.2 2.5% |

*Met the total acceptance criteria of $\leq 14\%$

b. *Linearity/assay reportable range:*

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Value Assignment:

A revised value assignment study was conducted based on FDA recommendations. Value assignment was performed by 3 operators with each operator running 12 tests (3 test cuvette lots over 4 instruments). Studies were performed in three runs using a different reagent cuvette lot for both ACT+ and ACT-LR. Results of each run must meet a $\leq 5\%$ error rate to be considered passing. A failed run is tested no more than twice under the same conditions. If the lot run fails after 2 additional runs, the lot is rejected and deleted from production. Each run must meet a pre-defined target range based on a 98% confidence level during validation of the product and aligned with literature based therapeutic ranges for ACT. Target ranges are as follows:

| Assay | Mean Target Range |
|----------------|-------------------|
| ACT+ Level 1 | 135-180 |
| ACT+ Level 2 | 347-500 |
| ACT-LR Level 1 | 103-157 |
| ACT-LR Level 2 | 190-312 |

The mean, SD and %CV is calculated for each passing lot. A standard factor (Total SD from the extended precision study) is used to account for inherent variability of the controls and for calculation of the reference range of each passing lot using the following formula:

$$\text{Mean clotting time of lot} \pm 2\text{SD} \times \text{total SD from the precision study}$$

Stability:

Two real time shelf life studies were conducted. The initial real time stability study demonstrated stability performance of ACT+ Level 1 and 2 controls,

and a revised study was conducted for the ACT-LR Level 1 and 2 controls.

Real time shelf life stability studies are currently ongoing for ACT-LR. The shelf life stability claim is based on real time stability data available at time of clearance for ACT-LR controls. For each level of controls, 3 lots of control material were stored at 2-8°C and tested 30 times at time zero and 10 times at multiple intermediate time points. The calculated mean, SD, %CV of each time point is compared against the baseline with acceptance criteria of $\pm 20\%$ maximum allowed deviation from the baseline.

Real time room temperature claim- one lot of each control level was tested 15 times at each time point: 0, 2, 3, 4 and 5 weeks. The baseline result and measurement at each time point must be within the pre-determined lot reference range for each lot tested in which the difference between the baseline and designated time points are $< 20\%$ maximum allowed deviation from the baseline.

All results met the predetermined acceptance criteria of ACT+ $< 12\%$ and ACT-LR $< 14\%$. The data therefore support the following shelf life stability at refrigerated storage between 2°C and 8°C and room temperature:

| Control Material | Shelf-life | Room temperature |
|------------------|------------|------------------|
| ACT+ Level 1 | 18 months | 4 weeks |
| ACT+ Level 2 | 18 months | 4 weeks |
| ACT-LR Level 1 | 5 months | 4 weeks |
| ACT-LR Level 2 | 5 months | 4 weeks |

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

Not applicable

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

Not applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. *Clinical specificity:*

Not applicable

c. *Other clinical supportive data (when a. and b. are not applicable):*

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Reference ranges will be available to customer on each package insert based on each lot of control that is manufactured.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.