Sensitive radioimmunoassay coated tube kit for the direct quantitative determination of total Estradiol-17β in human serum and plasma.

For In Vitro diagnostic Use

Kit content:
- Coated tubes: 2X50 tubes
- Tracer ≤ 85 kBq: 1 x 6 mL
- Calibrators 0 - 5: 6 x 2 mL
- Buffer for tracer & Incubation buffer: 1 x 45 mL
- Washing solution: 1 x 10 mL
- Plastic bag: 1
- Instruction For Use: 1

Warning: Some reagents contain sodium azide
1. INTENDED USE

ESTR-S-US is a highly sensitive radioimmunoassay coated tube kit for the direct quantitative determination of total Estradiol-17β in human serum or plasma.

The use of a highly sensitive estradiol-17β assay is necessary for young girls, peri- and post-menopausal women, and men. It is useful for testing young girls when precocious puberty is suspected. In post-menopausal women, concentrations of estradiol-17β are very low, similar to those found in men.

This low post-menopausal concentration increases the risk of osteoporosis and atherosclerosis, indicating the possible need for a hormone replacement therapy (HRT). In men, assays are useful in the investigation of feminizing syndromes (gynecomastia, estrogen-secreting tumors). Serum assays are a helpful tool for establishing the etiology of an amenorrhoea and/or sterility and in investigating estrogen-secreting tumors in women.

Finally, it is useful in monitoring ovulation induction.

2. INTRODUCTION

A steroid hormone, estradiol-17β is the most active oestrogen in the peripheral circulation. It is mainly produced in the ovary by the Graafian follicle.

A small amount is also produced by the adrenal cortex and by different tissues via the peripheral transformation of estrone and testosterone. In non-pregnant women, the estradiol-17β concentration varies with the menstrual cycle, the highest values generally occurring one day before ovulation.

This retro-control influence is vital in triggering the mid-cycle LH peak and therefore the ovulation. In the peripheral circulation, estradiol-17β is mainly present bound to proteins, the two most important being SHBG and albumin. The free form is physiologically active.

3. PRINCIPLE OF THE ASSAY

The principle of the assay is based on a two-step technique, using a solid phase.

In the first step, calibrators and samples are incubated in tubes coated with a high affinity anti-Estradiol antibody. After incubation, an amount of hormone proportional to the concentration of the Estradiol fraction present in the sample is bound to the bottom of the tubes.

In the second step, a 125I-Estradiol solution is added in the tube to saturate the remaining free antibody sites. Any unbound tracer is then removed.

The quantity of labelled Estradiol bound to the antibody is inversely related to the amount of unlabelled Estradiol present in the sample.

4. REAGENTS

Each kit contains enough reagents for 100 tubes. The expiry date is marked on the external label.

<table>
<thead>
<tr>
<th>REAGENTS</th>
<th>SYMBOLS</th>
<th>QUANTITY</th>
<th>STORAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>COATED TUBES: ready to use.</td>
<td>CT</td>
<td>2X50 tubes</td>
<td>2-8°C until the expiry date. Unused coated tubes removed from their bags should be stored in plastic bag supplied with the kit.</td>
</tr>
<tr>
<td>Rabbit anti-Estradiol antibodies coated at the bottom of the tube.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>125I-ESTRADIOL: concentrated solution.</td>
<td>TRACER</td>
<td>1 mL vial</td>
<td>2-8°C until the expiry date. 2-8°C up to 8 weeks after dilution within the limits of the expiry date of the kit. Return the tracer to 2-8°C immediately after use.</td>
</tr>
<tr>
<td>125I labelled ESTRADIOL, buffer (Sodium Dihydrogen Phosphate, glycerol, acetonitrile, sodium hydroxide, water) dye, and preservative. ≤ 85 kBq (≤ 2.3 μCi).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CALIBRATOR 0: ready to use.</td>
<td>CAL</td>
<td>1 mL vial</td>
<td>2-8°C until the expiry date.</td>
</tr>
<tr>
<td>Bovine serum, preservative and sodium azide.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CALIBRATORS 1 to 5: ready to use.</td>
<td>CAL</td>
<td>5 mL vials</td>
<td>2-8°C until the expiry date.</td>
</tr>
<tr>
<td>Estradiol (see below for concentrations), human serum, preservative and sodium azide. 10 - 25 - 100 - 500 - 2000 pmol/L (*)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUFFER: to be used for tracer dilution and incubation buffer: ready to use. Buffer (sodium dihydrogen phosphate, sodium hydroxide, tween 20, testosterone, water) and preservative.</td>
<td>BUF</td>
<td>1 mL vial</td>
<td>2-8°C until the expiry date.</td>
</tr>
</tbody>
</table>
WASHING SOLUTION: concentrated solution
Distilled water, detergent.

TWEEN 20
10 mL vial
2-8°C until the expiry date
After dilution store in a sealed container up to maximum 15 days within the limits of the expiry date of the kit (2-8°C).

PLASTIC BAG
1

(*) The values shown above are the target values. Real values of calibrators are indicated on the labels.

5. WARNING AND PRECAUTIONS

Safety measures
Raw materials of human origin contained in the reagents of this kit have been tested with licensed kits and found negative for the anti-HIV 1, anti-HIV 2, anti-HCV antibodies and the HBs antigen. However, as it is impossible to strictly guarantee that such products will not transmit hepatitis, the HIV virus, or any other viral infection, all raw materials of human origin including the samples to be assayed must be treated as potentially infectious.

All animal products are derivatives have been collected from healthy animals. Bovine components originate from countries where BSE has not been reported. Nevertheless, components containing animal substances should be treated as potentially infectious.

It is highly recommended to consider the following recommendations when using in vitro assays:
- Do not pipette by mouth.
- Do not smoke, eat or drink in areas in which specimens or kit reagents are handled.
- Wear disposable gloves while handling kit reagents or specimens and wash hands thoroughly afterwards.
- Avoid splashing.
- Decontaminate and dispose of specimens and all potentially contaminated materials as if they contained infectious agents.

The recommended method of doing this is autoclaving for a minimum of one hour at 121.5°C.

Sodium azide may react with lead or copper piping to form highly explosive metal azides. During waste disposal, flush the drains thoroughly to prevent a build-up of these products.

Basic radioprotection rules
This radioactive product may only be received, purchased, stored or used by persons so authorized, and by laboratories covered by such authorization. The solution should under no circumstances be administered to humans or to animals.

The purchase, storage, use or exchange of radioactive products are subject to the laws in force in the user's country.

The enforcement of the basic rules for handling radioactive products ensures adequate security.

A summary of these is given below:
- Radioactive products must be stored in their original containers in a suitable area.
- A record of the reception and storage of radioactive products must be kept up to date.
- Handling of radioactive products should take place in a suitably-equipped area with restricted access (controlled zone).
- Do not eat, drink, smoke or apply cosmetics in a controlled zone.
- Do not mouth-pipette radioactive solutions.
- Avoid any direct contact with all radioactive products by using laboratory coats and protective gloves.
- Contaminated laboratory equipment and glassware must be disposed of immediately after contamination to prevent cross-contamination of different isotopes.
- Any contamination or radioactive substance loss should be dealt with in accordance with the established procedures.
- All radioactive waste disposal must be carried out according to the regulations in force.

ESTR-S-US kit is intended for in vitro diagnostic use.
ESTR-S-US kit is intended for health professional only.
ESTR-S-US is not intended to be used with automated systems

6. DILUTION AND RECONSTITUTION

Dilutions
Samples: If elevated Estradiol levels are suspected, a diluent (ref: 1DIL-ESTR-US) is available on request (2 mL vial). A set of 5 additional diluent vials can be ordered separately under the reference: 5DIL-ESTR-US. It is recommended that disposable plastic tubes be used when carrying out the dilutions.
Tracer: Dilute the tracer 2.5 times with the buffer (e.g. 1ml tracer + 1.5 mL buffer). Recap the vial. Mix gently to ensure complete dilution. It is recommended that only the required volume of tracer be diluted at any time. It must be refrigerated immediately after use.
Washing solution: Dilute 1/333 the concentrated washing solution with distilled water (1.5 mL in 498.5 mL of distilled water to a final volume of 500 mL water). Cap the vial and mix.

Reconstitutions
All reagents are supplied in liquid form, no reconstitution is required

7. STORAGE INSTRUCTIONS

The kit is shipped at room temperature and should be stored at 2°-8°C. Keep away from heat our direct sun light. The storage and stability period of each reagent (inclusive of reconstituted reagents) are indicated in section 4 of the instructions for use leaflet.
8. SPECIMEN COLLECTION AND PREPARATION

The assay is performed on human sera or plasma (heparin or EDTA).

Warning:
- Do not use citrate plasma samples.
- Haemolysed oder hyperlipemic samples should not be used.

If the test is to be carried out within two days, the samples must be refrigerated at 2-8°C. Otherwise, they should be divided into aliquots, and stored deep frozen (-20°C) until needed (maximum 1 month). They must be thawed only just before using. Do not refreeze samples for later use.

9. ASSAY PROCEDURE

Material required but not provided
The following material is required but not provided in the kit (refer to section 4 for the list of reagents provided in the kit):
- Precision micropipettes or similar, with disposable tips, capable of dispensing 100 µL, 200 µL, 250 µL and 2 mL. Their calibrations should be checked regularly.
- Reagent dispenser 1 mL (for washing)
- Distilled water.
- Diluent for dilution of elevated Estradiol levels ref: 1DIL-ESTR-US (2 mL vial), or 5DIL-ESTR-US (5 x 2 mL vials).
- Vortex type mixer.
- Absorbent paper.
- Water bath (37°C).
- Parafilm (optional).
- Disposable plastic test-tubes.
- Gamma scintillation counter calibrated for 125 Iodine.

Handling precautions
- Before starting the assay, read completely and carefully the instructions for use. Use the version of the package insert provided with the kit. Be sure that everything is understood prior starting.
- Do not use kit components beyond their expiry date.
- Do not mix reagents from different batches.
- Follow good laboratory practices and safety guidances.
- Do not contaminate kit components and pipette tips with estradiol from an external source (e.g. hormone gel).
- Avoid any microbial contamination of the reagents or if the water used for washing.
- Follow reasonable precautions to avoid introduction of significant quantities of microorganisms.
- Fully respect the incubation times and the washing instructions.
- All reagents must be brought to room temperature (18-25°C) at least 30 minutes before their use. Dispensing of reagents is also carried out at room temperature.

The assay requires the following groups of tubes:
- T group, for the total activity determination.
- Calibrator groups, to establish the calibration curve.
- Sx groups, for the test samples.

It is recommended to perform the assay in duplicate for the calibrator groups and samples.

Protocol
Strictly observe the order in which reagents have to be added.
1- Dispense 200 µL of calibrators and samples to be assayed into the corresponding labeled coated tubes.
2- Add 250 µL of buffer to each tube (except T group).
3- Mix each tube gently with a Vortex-type mixer.
4- Incubate 1 hour at 37°C after covering the tubes with plastic film.
5- Add 100 µL of 125I-Estradiol to each tube (and T group). Return the remaining tracer to the refrigerator.
6- Mix each tube gently with a Vortex-type mixer.
7- Cover the tubes with plastic film and Incubate 1 hour at 37°C.
8- Decant liquid from each assay tube and tap the head of each tube firmly onto absorbent paper.
9- Wash once with 1 mL of washing solution (except T tubes), shaking the rack by hand.
10- Empty the tubes and tap firmly onto absorbent paper. Let the tubes stand upside down at least 5 min. (except T tubes).
11- Measure (for at least 2 minutes) the remaining radioactivity bound to the tubes with a gamma scintillation counter calibrated for 125 Iodine.
**Assay flowchart**

<table>
<thead>
<tr>
<th>Groups of tubes</th>
<th>Volume (in µL) of Calibrators Controls or Samples to add in the tubes</th>
<th>Mix &amp; Incubation</th>
<th>Volume (in µL) of Buffer to add in the tubes</th>
<th>Volume (in µL) of 125I Estradiol to add in the tubes</th>
<th>Mix, incubation and reagents removal</th>
<th>Volume (in µL) of Washing solution to add in the tubes</th>
<th>Reagent removal and count</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total activity (T)</strong></td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>100</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Calibrators</td>
<td>200</td>
<td>Mix</td>
<td>Incubate 1h at 37°C</td>
<td>100</td>
<td>Mix</td>
<td>Incubate 1h at 37°C</td>
<td>1000</td>
</tr>
<tr>
<td>Samples (Sx)</td>
<td>200</td>
<td>250</td>
<td>200</td>
<td>250</td>
<td>1000</td>
<td>Measure for at least 2 minutes</td>
<td></td>
</tr>
</tbody>
</table>

**Calibration**

Values of the calibrators and controls are assigned against an in-house master calibrator set prepared by gravimetry. Calibrator traceability is performed to the reference method, Isotope Dilution Mass spectrometry (IDMS). The limit of detection of the assay was assessed at 5 pmol/L.

Good laboratory practices require the use of quality control samples in each series of assays to check the quality of the results obtained. All specimens should be treated identically, and result analysis using the appropriate statistical methods is recommended. Test results are valid only if the test has been performed following the instructions. Moreover, the user must strictly adhere to the rules of GLP or other applicable federal, state and local standards and/or law. All calibrators and controls must be found within the acceptable ranges as stated on the quality control certificate. If the criteria are not met, the run is not valid and should be repeated. It is recommended to take part to appropriate quality control trials.

In order to establish the calibration curve, the following procedure must be followed:

- Determine the mean value for counts of each duplicate after subtracting the background.
- Express in counts per minute (or in B/B0(%) the bound activity of each calibrator, control and sample.
- Calculate the percent binding B/B0(%) for each calibrator, sample and control as follows:

\[
B/B0(\%) = \frac{\text{Counts (Calibrator or sample)}}{\text{Counts (Zero Calibrator)}} \times 100
\]

- The obtained B/B0 (%) of the calibrators (y-axis, linear) are plotted against their concentration (x-axis, semi logarithmic).
- For the calculation of the calibration curve, apply each signal of the calibrators (one obvious outlier of duplicates might be omitted and the more plausible single value might be used), the mathematical fit “forced spline” must be applied in order to establish the calibration curve.

Conversion to pg/ml may be accomplished by using the following equation:

\[
\text{Estradiol (pg/mL)} = \text{Estradiol (pmol/L)} \times 0.2724
\]

**Typical calibration curve** (example only): these data must not be substituted for results obtained in the laboratory

<table>
<thead>
<tr>
<th>GROUPS OF TUBES</th>
<th>Mean CPM</th>
<th>B/Bo x 100</th>
<th>Concentration pmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>13370</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Calibrator 0</td>
<td>0 pmol/L</td>
<td>4730</td>
<td>100</td>
</tr>
<tr>
<td>Calibrator 1</td>
<td>10 pmol/L</td>
<td>4250</td>
<td>89.4</td>
</tr>
<tr>
<td>Calibrator 2</td>
<td>25 pmol/L</td>
<td>3741</td>
<td>79.1</td>
</tr>
<tr>
<td>Calibrator 3</td>
<td>100 pmol/L</td>
<td>2624</td>
<td>55.5</td>
</tr>
<tr>
<td>Calibrator 4</td>
<td>500 pmol/L</td>
<td>875</td>
<td>18.5</td>
</tr>
<tr>
<td>Calibrator 5</td>
<td>2000 pmol/L</td>
<td>349</td>
<td>7.8</td>
</tr>
<tr>
<td>Sample A</td>
<td>2548</td>
<td>53.9</td>
<td>84/4</td>
</tr>
<tr>
<td>Sample B</td>
<td>575</td>
<td>12.2</td>
<td></td>
</tr>
</tbody>
</table>

**Results**

The estradiol concentrations of the samples are determined by interpolation of the sample values from the calibration curve. The concentration is read directly on the x-axis. Correct the read value for the dilution factor, if necessary.

Conversion to pg/ml may be accomplished by using the following equation:

\[
\text{Estradiol (pg/mL)} = \text{Estradiol (pmol/L)} \times 0.2724
\]
10. LIMITATION OF THE METHOD

Strict following of the procedures described in this package insert and careful handling of the reagents will enable reliable results to be obtained with the ESTR-S-US kit. Do not attempt to extrapolate sample values beyond the last calibrator. Samples showing concentration above the highest calibrator should be diluted the samples and re-assayed.

11. EXPECTED VALUES

Each laboratory must establish its own range of normal values. Estradiol values were followed during one menstrual cycle in 25 healthy, normally menstruating women. The ovulation days were established by measuring the LH value of each sample. Day 0 is the day of the LH peak. Results are shown in table below:

<table>
<thead>
<tr>
<th>Phases</th>
<th>Days from the LH peak</th>
<th>n</th>
<th>Mean (pmol/L)</th>
<th>Range (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular</td>
<td>-8</td>
<td>10</td>
<td>150</td>
<td>105-217</td>
</tr>
<tr>
<td></td>
<td>-4</td>
<td>15</td>
<td>343</td>
<td>207-1000</td>
</tr>
<tr>
<td>Mid-cycle</td>
<td>-1</td>
<td>24</td>
<td>709</td>
<td>416-1399</td>
</tr>
<tr>
<td>Luteal phase</td>
<td>9</td>
<td>17</td>
<td>399</td>
<td>165-788</td>
</tr>
</tbody>
</table>

Serum Estradiol values were also measured in samples from 42 post-menopausal women without hormone replacement therapy, 42 pre-pubertal girls and 117 apparently healthy men. Results are shown in the tables below:

**Women**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>n</th>
<th>Mean (pmol/L)</th>
<th>Range (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenopausal women</td>
<td>47-66 years</td>
<td>42</td>
<td>26</td>
<td>11-50</td>
</tr>
<tr>
<td>Pre-pubertal girls</td>
<td>3-5 years</td>
<td>42</td>
<td>17</td>
<td>ND-36</td>
</tr>
</tbody>
</table>

**Men**

<table>
<thead>
<tr>
<th>n = 117</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean = 117 pmol/L</td>
</tr>
<tr>
<td>Reference interval* = 34-226 pmol/L</td>
</tr>
<tr>
<td>Confidence interval = 90%</td>
</tr>
<tr>
<td>Lower reference limit = 23 – 51 pmol/L</td>
</tr>
<tr>
<td>Upper reference limit = 191 – 266 pmol/L</td>
</tr>
</tbody>
</table>

ND = non detectable

* Reference interval = 2.5 and 97.5 percentiles.

12. SPECIFIC PERFORMANCES

**Precision**

This was evaluated using 8 samples with different concentrations assayed 10 times in the same series or in duplicate in 10 different series.

<table>
<thead>
<tr>
<th>Samples</th>
<th>Mean value (pmol/L)</th>
<th>CV (%)</th>
<th>Samples</th>
<th>Mean value (pmol/L)</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17</td>
<td>18.1</td>
<td>5</td>
<td>12</td>
<td>17.6</td>
</tr>
<tr>
<td>2</td>
<td>87</td>
<td>2.8</td>
<td>6</td>
<td>94</td>
<td>5.8</td>
</tr>
<tr>
<td>3</td>
<td>311</td>
<td>3.5</td>
<td>7</td>
<td>260</td>
<td>8.1</td>
</tr>
<tr>
<td>4</td>
<td>1021</td>
<td>5</td>
<td>8</td>
<td>1799</td>
<td>9.7</td>
</tr>
</tbody>
</table>

**Recovery**

Known quantities of Estradiol were added to different serum pools. The recovery percentages of ESTR-S-US obtained were in the range from 88% to 117%, with a mean value of 102%.

with high levels were diluted, with the recovery percentages ranging from 90 to 110 %.

**Specificity**

This was determined from equivalent displacement measurements at 50% binding. The antiserum used in the test showed the following cross-reactions:
<table>
<thead>
<tr>
<th>Compound</th>
<th>Cross reactivity (%)</th>
<th>Compound</th>
<th>Cross reactivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>100</td>
<td>Estrone-glucuronide, sodium salt</td>
<td>0.004</td>
</tr>
<tr>
<td>Equilenin</td>
<td>8.9</td>
<td>Norethisterone acetate</td>
<td>0.002</td>
</tr>
<tr>
<td>Ethinylestradiol</td>
<td>1.4</td>
<td>Mesterolone</td>
<td>0.002</td>
</tr>
<tr>
<td>Equilin</td>
<td>1.1</td>
<td>Norgestrel</td>
<td>0.001</td>
</tr>
<tr>
<td>Estrone</td>
<td>0.97</td>
<td>Estradiol-3, 17-disulphate, disodium salt</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>16-Oxoestradiol</td>
<td>0.86</td>
<td>Estradiol-17-sulphate, sodium salt</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estradiol-3-glucuronide, sodium salt</td>
<td>0.61</td>
<td>Testosterone</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Estradiol</td>
<td>0.44</td>
<td>Cortisol</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>16-hydroxyestrone</td>
<td>0.26</td>
<td>Cortisone</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Estradiol-17-glucuronide, sodium salt</td>
<td>0.25</td>
<td>Ethisterone</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Estradiol-17-valerate</td>
<td>0.16</td>
<td>Danazol</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Progesterone</td>
<td>&lt; 0.05</td>
<td>3,17-Beta-D-glucuroconjugate</td>
<td>0.007</td>
</tr>
<tr>
<td>Corticosterone</td>
<td>0.02</td>
<td>Androstenediol</td>
<td>&lt; 0.0003</td>
</tr>
<tr>
<td>Estradiol-3-sulfate</td>
<td>0.02</td>
<td>Oestrone-3-Beta-D-glucuronide</td>
<td>0.0003</td>
</tr>
<tr>
<td>2-hydroxyestradiol</td>
<td>0.01</td>
<td>Oestrone-3-sulfate</td>
<td>&lt;0.0003</td>
</tr>
<tr>
<td>Norethisterone</td>
<td>0.01</td>
<td>17α-Estradiol</td>
<td>0.005</td>
</tr>
</tbody>
</table>

The Tamoxifen and Fulvestran (FASLODEX®) drugs at a respective concentration of 8µg/mL and 25ng/mL do not interfere with the ESTR-S-US assay.

**Interferences**

No interference with bilirubin, hemoglobin and SHBG measured up to respective concentrations of equal to 170 µmol/L, 10 g/L and 2000 nmol/L, has been observed.

Addition of lipids lowers measured concentrations and therefore, the use of highly lipemic samples is not recommended.

**Detection limit**

The detection limit is defined as being the smallest concentration different from the zero with a probability of 95%. It has been assessed as being 5 pmol/L.

### 13. BIBLIOGRAPHY


Jones SG. Endocrine review. 1984;5:62-75.


### 14. SYMBOLS

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Meaning of symbols</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE</td>
<td>CE mark - Compliance with European Regulation</td>
</tr>
<tr>
<td></td>
<td>Storage temperature limitation</td>
</tr>
<tr>
<td>LOT</td>
<td>Batch number</td>
</tr>
<tr>
<td></td>
<td>Use by date</td>
</tr>
<tr>
<td></td>
<td>Read the instructions for use</td>
</tr>
</tbody>
</table>
15. MANUFACTURER AND DISTRIBUTOR IDENTIFICATION & LAST REVISION


ESTR-S-US kit is distributed in the US by ALPCO Diagnostic, Inc located 26-G Keewaydin Dr. Salem, NH 03079, USA.

Last revision of the instructions for use: version 22 from June 2017.