

**Date: 26 April 2019**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**Montek, radionuclide generator**

**1. NAME OF THE MEDICINAL PRODUCT**

Montek

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Sodium pertechnetate (99mTc) injection is produced by means of a (99Mo/99mTc) generator. Technetium (99mTc) decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6.01 hours to technetium (99Tc) which, in view of its long half-life of 2.13 x 105 years, can be regarded as quasi stable.

The radionuclide generator containing the parent isotope 99Mo, adsorbed on a chromatographic column delivers sodium pertechnetate (99mTc) injection in sterile solution.

The 99Mo on the column is in equilibrium with the formed daughter isotope 99mTc. The generators are supplied with the following 99Mo activity amounts at activity reference time which deliver the following technetium (99mTc) amounts, assuming a 100% theoretical elution yield and 24 hours time from previous elution and taking into account that branching ratio of 99Mo is about 87%:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 99mTc activity (Maximal theoretical eluable activity atcalibration date, 8 A.M. GMT +3) | 8.3 | 12.6 | 16.8 | 21.1 | 25.3 | 29.6 | 33.9 | GBq |
| 99Mo activity (at calibration date, 8 A.M. GMT +3) | 10 | 15 | 20 | 25 | 30 | 35 | 40 | GBq |

The technetium (99mTc) amounts available by a single elution depend on the real yields of the kind of generator used itself declared by manufacturer and approved by NCA.

Excipient(s) with known effect:

Each mL of sodium pertechnetate (99mTc) solution contains 3.54 mg of sodium.

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Radionuclide generator

Blue colour, plastic covered, cylindrical body and closure, attached to the body with 2 clamps, with a holder on top.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

This medicinal product is for diagnostic use only.

The eluate from the radionuclide generator (sodium pertechnetate (99mTc) injection), is indicated for: labelling of various kits for radiopharmaceutical preparation developed and approved for radiolabelling with such solution.

Thyroid scintigraphy: direct imaging and measurement of thyroid uptake to give information on the size, position, nodularity and function of the gland in case of thyroid disease.

Salivary gland scintigraphy: diagnosis of chronic sialadenitis (e.g. (Sjögren's Syndrom) as well as assessment of salivary gland function and duct patency in salivary glands disorders and monitoring of the response to therapeutic interventions (in particular radio iodine therapy).

Location of ectopic gastric mucosa (Meckel’s diverticulum)

Lacrimal duct scintigraphy: to assess functional disorders of lacrimation and monitoring of the response to therapeutic interventions.

**4.2 Posology and method of administration**

Posology

If sodium pertechnetate (99mTc) solution is administered intravenously, activities may vary widely according to the clinical information required and the equipment employed. The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified for certain indications. Recommended activities are as follows:

 Recommended activities are as follows:

 *Adults (70 kg) and the elderly population*

* Thyroid scintigraphy: 20-80MBq.
* Salivary gland scintigraphy: 30 to 150 MBq for static images up to 370 MBq for dynamic images
* Meckel’s diverticulum scintigraphy: 300- 400 MBq.
* Lacrimal duct scintigraphy: 2-4 MBq per drop per eye.

*Renal impairment*

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

*Paediatric population*

The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

The activity to be administered to children and adolescents may be calculated according to the recommendations of European Association Nuclear Medicine (EANM) paediatric dosage card; the activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the weight-dependent correction factor given in the table below (see Table 1):

A[MBq]Administered = Baseline Activity × Multiple

*Thyroid scintigraphy*

Activity administered [MBq] = 5.6 MBq x correction factor (Table 1). A minimal activity of 10 MBq is necessary for obtaining images of sufficient quality.

*Identification/location of ectopic gastric mucosa*

Activity administered [MBq] = 10.5 MBq x correction factor (Table 1). A minimal activity of 20 MBq is necessary in order to obtain images of sufficient quality.

**Table 1:** Weight-dependent correction factors in the paediatric population (for thyroid scintigraphy and identification/location of ectopic gastric mucosa) according to the EANM-May 2008 guidelines

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Weight****[kg]** | Multiple | **Weight****[kg]** | Multiple | **Weight****[kg]** | Multiple |
| **3** | 1 | **22** | 5.29 | **42** | 9.14 |
| **4** | 1.14 | **24** | 5.71 | **44** | 9.57 |
| **6** | 1.71 | **26** | 6.14 | **46** | 10.00 |
| **8** | 2.14 | **28** | 6.43 | **48** | 10.29 |
| **10** | 2.71 | **30** | 6.86 | **50** | 10.71 |
| **12** | 3.14 | **32** | 7.29 | **52-54** | 11.29 |
| **14** | 3.57 | **34** | 7.72 | **56-58** | 12.00 |
| **16** | 4.00 | **36** | 8.00 | **60-62** | 12.71 |
| **18** | 4.43 | **38** | 8.43 | **64-66** | 13.43 |
| **20** | 4.86 | **40** | 8.86 | **68** | 14.00 |

*Salivary gland scintigraphy*

The Paediatric Task Group of EANM (1990) recommends that the activity to be administered to a child should be calculated from the body weight according to the table below (see Table 2) with a minimum dose of 10 MBq in order to obtain images of sufficient quality.

**Table 2:** Weight-dependent correction factor in the paediatric population (for salivary gland scintigraphy) according to EANM 1990 recommendations

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Weight****[kg]** | Factor | **Weight****[kg]** | Factor | **Weight****[kg]** | Factor |
| **3** | 0.1 | **22** | 0.50  | **42** | 0.78 |
| **4** | 0.14 | **24** | 0.53 | **44** | 0.80 |
| **6** | 0.19 | **26** | 0.56 | **46** | 0.82 |
| **8** | 0.23 | **28** | 0.58 | **48** | 0.85 |
| **10** | 0.27 | **30** | 0.62 | **50** | 0.88 |
| **12** | 0.32 | **32** | 0.65 | **52-54** | 0.90 |
| **14** | 0.36 | **34** | 0.68 | **56-58** | 0.92 |
| **16** | 0.40 | **36** | 0.71 | **60-62** | 0.96 |
| **18** | 0.44 | **38** | 0.73 | **64-66** | 0.98 |
| **20** | 0.46 | **40** | 0.76 | **68** | 0.99 |

*Lacrimal duct scintigraphy*

Recommended activities apply as well for adults as for children.

Method of administration

For intravenous or ocular use.

For multidose use.

For instructions on extemporaneous preparation of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

In thyroid scintigraphy, salivary gland scintigraphy and identification/location of ectopic gastric mucosa, the sodium pertechnetate (99mTc) solution is administered by intravenous injection.

In lacrimal duct scintigraphy, drops are instilled in each eye (ocular use).

Image acquisition

Thyroid scintigraphy: 20 minutes after intravenous injection.

Salivary gland scintigraphy: immediately after intravenous injection and at regular intervals for 15 minutes.

Identification/location of ectopic gastric mucosa (Meckel’s Diverticulum): immediately after intravenous injection and at regular intervals for 30 minutes.

Lacrimal duct scintigraphy: dynamic acquisition within 2 minutes after instillation, followed by static images acquired at regular intervals within 20 minutes.

**4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

**4.4 Special warnings and precautions for use**

Potential for hypersensitivity or anaphylactic reactions

If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification

For each patient, radiation exposure must be justifiable by the likely benefit. The activity administered should be in every case as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population

For information on the use in paediatric population, see section 4.2.

Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Thyroid blocking is of special importance in the paediatric patient population except for thyroid scintigraphy.

Patient preparation

Pre-treatment of patients with thyroid-blocking medicinal products may be necessary for certain indications.

The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

To avoid false positives or to minimise irradiation by reduction of pertechnetate accumulation in the thyroid and salivary glands, a thyroid blocking agent should be given prior to lacrimal duct scintigraphy or Meckel’s diverticulum scintigraphy. Conversely a thyroid blocking agent must NOT be used before thyroid, parathyroid or salivary glands scintigraphy.

Before the application of sodium pertechnetate (99mTc) solution for scintigraphy of Meckel’s diverticulum the patient must keep an empty stomach for 3 to 4 hours to reduce intestinal peristalsis.

After *in vivo* labelling of erythrocytes using stannous ions for reduction sodium pertechnetate (99mTc) is primarily built into erythrocytes, therefore Meckel’s scintigraphy should be performed before or some days after *in vivo* labelling of erythrocytes.

After the procedure

Close contact with infants and pregnant women should be restricted during 12 hours.

Specific warnings

Sodium pertechnetate (99mTc) solution for injection contains 3.54 mg/ml of sodium.

Depending on the time when the injection is administered, the content of sodium given to the patient may in some cases be greater than 1 mmol (23 mg). This should be taken into account in patient on low sodium diet.

When sodium pertechnetate (99mTc) solution is used for labelling of a kit, the determination of the overall sodium content must take into account the sodium derived from the eluate and the kit. Please refer to the package leaflet of the kit.

In salivary gland scintigraphy a lower specificity of the method should be expected compared to magnetic resonance sialography.

For precautions with respect to environmental hazard see section 6.6.

**4.5 Interaction with other medicinal products and other forms of interaction**

Atropine, isoprenaline and analgesics may cause a delay in gastric emptying and thereby cause a redistribution of (99mTc)pertechnetate in abdominal imaging.

Administration of laxatives should be withheld since they irritate the gastrointestinal tract. Contrast-enhanced studies (e.g. barium) and upper gastro-intestinal examination should be avoided within 48h prior to administration of pertechnetate (99mTc) for Meckel’s diverticulum scintigraphy.

Many pharmacological medicinal products are known to modify the thyroid uptake.

* antithyroid medicinal products (e.g. carbimazole or other imidazole derivatives such as propylthiouracil), salicylates, steroids, sodium nitroprusside, sodium sulfobromophtalein, perchlorate should be withheld for 1 week prior thyroid scintigraphy;
* phenylbutazone and expectorants should be withheld for 2 weeks;
* natural or synthetic thyroid preparations (e.g. sodium thyroxine, sodium liothyronine, thyroid extract) should be withheld for 2-3 weeks
* amiodarone, benzodiazepines, lithium should be withheld for 4 weeks
* intravenous contrast agents should not have been administered within 1-2 months.

**4.6 Pregnancy and lactation**

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

Administration of pertechnetate (99mTc) to a woman who is known to be pregnant should be justified by medical need and a positive individual benefit risk assessment for the mother and the foetus.

Alternative non-irradiating diagnostic modalities should be taken into account.

99mTc (as free pertechnetate) has been shown to cross the placental barrier.

Breast-feeding

Before administering radiopharmaceuticals to a woman who is breast-feeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be interrupted for 12 hours post administration and the expressed feeds discarded.

Close contact with infants should be restricted during this period.

**4.7 Effects on ability to drive and use machines**

Sodium pertechnetate (99mTc) solution has no influence on the ability to drive and use machines.

**4.8 Undesirable effects**

Summary of the safety profile

Information on adverse reactions is available from spontaneous reporting. The reported reaction types are anaphylactoid reactions, vegetative reactions, as well as different kinds of injection site reactions.

Sodium pertechnetate (99mTc) from the MONTEK radionuclide generator is used for radioactive labelling of a variety of compounds. These medicinal products generally have a higher potential for adverse reactions than 99mTc, and therefore the reported adverse reactions are rather related to the labelled compounds than to 99mTc. The possible types of adverse reactions following intravenous administration of 99mTc -labelled pharmaceutical preparation will be dependent on the specific compound being used. Such information can be found in the SmPC of the kit used for radiopharmaceutical preparation.

Tabulated list of adverse reactions

The frequencies of undesirable effects are defined as follows:

Not known (cannot be estimated from the available data).

*Immune system disorder*

Frequency unknown\*: Anaphylactoid reactions (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various location e.g. face oedema)

*Nervous system disorders*

Frequency unknown\*: Vasovagal reactions (e.g. syncope, tachycardia, bradycardia, dizziness, headache, vision blurred, flushing)

*Gastrointestinal disorders*

Frequency unknown\*: Vomiting, nausea, diarrhoea

*General disorders and administration site conditions*

Frequency unknown\*: Injection site reactions due to extravasation (e.g. cellulitis, pain, erythema, swelling)

\* Adverse reactions derived from spontaneous reporting

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 5.2 mSv when the maximal recommended activity of 400 MBq is administered these adverse reactions are expected to occur with a low probability.

Description of selected adverse reactions

*Anaphylactic reactions* (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various locations [e.g. face oedema])

Anaphylactic reactions have been reported following intravenous injection of sodium perchtechnetate (99mTc) and include various skin or respiratory symptoms like skin irritations, oedema, or dyspnoea.

*Vegetative reactions (nervous system and gastrointestinal disorders)*

Single cases of severe vegetative reactions have been reported, however, most of the reported vegetative reactions include gastrointestinal reactions like nausea or vomiting. Other reports include vasovagal reactions like headache or dizziness. Vegetative reactions are rather considered to be related to the examinational setting than to technetium (99mTc), especially in anxious patients.

*General disorders and administration site conditions*

Other reports describe local injection site reactions. Such reactions are related to extravasation of the radioactive material during the injection, and the reported reactions rank from local swelling up to cellulitis. Depending on the administered radioactivity and the labeled compound, extended extravasation may necessitate surgical treatment.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Danish Medicines Agency

Axel Heides Gade 1

DK-2300 København S

Websted: [www.meldenbivirkning.dk](http://www.meldenbivirkning.dk)

E-mail: dkma@dkma.dk

**4.9 Overdose**

In the event of the administration of a radiation overdose with sodium pertechnetate (99mTc), the absorbed dose should be reduced where possible by increasing the elimination of the radionuclide from the body by defaecation, forced diuresis and frequent bladder voiding.

The uptake in the thyroid, salivary glands and the gastric mucosa can be significantly reduced when sodium or potassium perchlorate is given immediately after an accidentally high dose of sodium pertechnetate (99mTc) was administered.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

ATC code: V 09 FX 01. Diagnostic radiopharmaceuticals, various thyroid diagnostic radiopharmaceuticals.

No pharmacological activity has been observed in the range of doses administered for diagnostic purposes.

**5.2 Pharmacokinetic properties**

Distribution

The pertechnetate ion has similar biological distribution to iodide and perchlorate ions, concentrating temporarily in salivary glands, choroid plexus, stomach (gastric mucosa) and in the thyroid gland, from which it is eliminated, unchanged. The pertechnetate ion also tends to concentrate in areas with increased vascularisation or with abnormal vascular permeability, particularly when pre-treatment with blocking agents inhibits uptake in glandular structures. With intact blood brain barrier, sodium pertechnetate (99mTc) does not penetrate into the brain tissue.

Organ uptake

In the blood 70-80% of the intravenously injected sodium pertechnetate (99mTc) is bound to proteins, primarily in an unspecific way to albumin. The unbound fraction (20-30%) accumulates temporarily in thyroid and salivary glands, stomach and nasal mucous membranes as well as in the plexus chorioideus.

Sodium pertechnetate (99mTc) in contrast to iodine, nevertheless, is neither used for the thyroid hormone synthesis (organification), nor absorbed in the small intestine. In the thyroid the maximum accumulation, depending on functional status and iodine saturation (in euthyroidism approx. 0.3-3%, in hyperthyroidism and iodine depletion up to 25%) is reached about 20 min after injection and then decreases quickly. This also applies for the stomach mucous membrane parietal cells and the salivary glands acinar cells.

In contrast to the thyroid, which releases sodium pertechnetate (99mTc) in the bloodstream, the salivary glands and the stomach secrete sodium pertechnetate (99mTc) in the saliva and gastric juice, respectively. The accumulation by the salivary gland lies in the magnitude of 0.5% of the applied activity with the maximum reached after about 20 minutes. One hour after injection, the concentration in the saliva is about 10-30 fold higher than in the plasma. The excretion can be accelerated by lemon juice or by stimulation of the parasympathetic nerve system, the absorption is reduced by perchlorate.

Elimination

Half life in plasma is approximately 3 hours. Sodium pertechnetate (99mTc) is not metabolised in the organism. One fraction is eliminated very quickly renally, the rest more slowly via faeces, salivary and tear liquid. Excretion during the first 24 hours following administration is mainly urinary (approximately 25 %) with faecal excretion occurring over the next 48 hours. Approximately 50 % of the administered activity is excreted within the first 50 hours. When selective uptake of pertechnetate (99mTc) in glandular structures is inhibited by the preadministration of blocking agents, excretion follows the same pathways but there is a higher renal clearance.

The above data are not valid when sodium pertechnetate (99mTc) is used for labelling of another radiopharmaceutical.

**5.3 Preclinical safety data**

There is no information on acute, subacute and chronic toxicity from single or repeated dose administration. The quantity of sodium pertechnetate (99mTc) administered during clinical diagnostic procedures is very small and, apart from allergic reactions, no other adverse reactions have been reported.

This medicinal product is not intended for regular or continous administration.

Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

Reproductive toxicity

Placental transfer of 99mTc from intravenously administered sodium pertechnetate (99mTc) has been studied in mice. The pregnant uterus was found to contain as much as 60% of the injected 99mTc when administered without perchlorate pre-administration. Studies performed on pregnant mice during gestation, gestation and lactation, and lactation alone showed changes in progeny, which included weight reduction, hairlessness and sterility.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Aluminium oxide

Molybdenum trioxide

Sodium hydroxide

Hydrogen peroxide 30 %

Sodium hydroxide 1 M (pH adjustment)

Hydrochloric acid 4 M (pH adjustment)

Hydrochloric acid 1 M (pH adjustment)

Sodium chloride 9 mg/ml (0.9%) solution for injection

Water for injections

**6.2 Incompatibilities**

This medicinal product must not be mixed with other medicinal products except for those mentioned in section 12.

**6.3 Shelf life**

Generator: 21 days from manufacturing date.

The calibration date and the expiry date are stated on the label.

Sodium pertechnetate (99mTc) eluate: After elution, use within 8 hours.

Elution vials: 24 months.

Solution for elution: 24 months.

**6.4 Special precautions for storage**

Store the generator and the eluate, Sodium Pertechnetate (99mTc) Injection below 25 °C in the original package.

Do not freeze.

Eluate: For storage conditions after elution of the medicinal product, see section 6.3.

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

**6.5 Nature and contents of container**

**Primary container**

Radionuclide Generator: Type I, colourless, natural glass column and bromobutyl rubber stopper, aluminium cap.

Evacuated vial: 20 ml colourless, Type I natural glass vial and bromobutyl rubber stopper, aluminium cap.

Sodium chloride 9 mg/ml (0.9%) solution for injection. 5 ml, 10 ml: colourless, 20 ml, Type I natural glass vial and bromobutyl rubber stopper, aluminium cap.

**Outer container**

A tin bucket with the aid of styrofoam filling material includes the following material:

Radionuclide generator: Lead shield in plastic outer container.

Evacuated vial: cardboard box

Sodium chloride 9 mg/ml (0.9%) solution for injection of 5 ml, 10 ml: cardboard box

**Accessories available**

Sodium chloride 9mg/ml (0.9%) solution for injection eluent vials

The sodium chloride 9 mg/ml (0.9%) solution for injection eluent is available in 2 different volumes giving elution volumes of 5 ml and 10 ml to allow the generator eluate to be collected at varying radioactive concentrations.

Packs of 5 vials containing 5 ml and 5 vials containing10 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection.

The following options are available according to custom order

Packs of 10 vials containing 5 ml sodium chloride 9 mg/ml (0.9%) solution for injection or 10 vials containing 10 ml sodium chloride 9 mg/ml (0.9%) solution for injection.

Vials are packed in 5 vial cartons.

**Evacuated elution vials**

Packs of 10 vials. Vials are packed in 5 vial cartons.

**6.6 Special precautions for disposal and other handling**

General warnings

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner, which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

If at any time the integrity of the generator or the vial with the eluted solution is compromised, it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

The residual activity of the generator must be estimated before disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

**7. MARKETING AUTHORISATION HOLDER**

Monrol Europe S.R.L

Pantelimon, Str. Gradinarilor, nr.1

077145 Ilfov

Romania

**8. MARKETING AUTHORISATION NUMBER(S)**

 DK R 02246

**9. DATE OF FIRST AUTHORISATION**

27 September 2011

**10. DATE OF REVISION OF THE TEXT**

 26 April 2019

**11. DOSIMETRY**

The data listed below are from ICRP 80 and are calculated according to the following assumptions:

**(I) Without pre-treatment with a blocking agent:**

|  |  |
| --- | --- |
| **Organ** | **Absorbed dose per administered unit of activity (mGy/MBq)** |
|  | **Adult** | **15 Year** | **10 Year** | **5 Year** | **1 Year** |
| Adrenals | 0.0037 | 0.0047 | 0.0072 | 0.011 | 0.019 |
| Bladder wall | 0.018 | 0.023 | 0.030 | 0.033 | 0.060 |
| Bone surfaces | 0.0054 | 0.0066 | 0.0097 | 0.014 | 0.026 |
| Brain | 0.0020 | 0.0025 | 0.0041 | 0.0066 | 0.012 |
| Breast | 0.0018 | 0.0023 | 0.0034 | 0.0056 | 0.011 |
| Gallbladder | 0.0074 | 0.0099 | 0.016 | 0.023 | 0.035 |
| Gastrointestinal tract |  |  |  |  |  |
|  - Stomach wall | 0.026 | 0.034 | 0.048 | 0.078 | 0.16 |
|  - Small intestine | 0.016 | 0.020 | 0.031 | 0.047 | 0.082 |
|  - Colon | 0.042 | 0.054 | 0.088 | 0.14 | 0.27 |
|  - Ascending colon wall | 0.057 | 0.073 | 0.12 | 0.20 | 0.38 |
|  - Descending colon wall | 0.021 | 0.028 | 0.045 | 0.072 | 0.13 |
| Heart | 0.0031 | 0.0040 | 0.0061 | 0.0092 | 0.017 |
| Kidneys | 0.0050 | 0.0060 | 0.0087 | 0.013 | 0.021 |
| Liver | 0.0038 | 0.0048 | 0.0081 | 0.013 | 0.022 |
| Lungs | 0.0026 | 0.0034 | 0.0051 | 0.0079 | 0.014 |
| Muscles | 0.0032 | 0.0040 | 0.0060 | 0.0090 | 0.016 |
| Oesophagus | 0.0024 | 0.0032 | 0.0047 | 0.0075 | 0.014 |
| Ovaries | 0.010 | 0.013 | 0.018 | 0.026 | 0.045 |
| Pancreas | 0.0056 | 0.0073 | 0.011 | 0.016 | 0.027 |
| Red bone marrow | 0.0036 | 0.0045 | 0.0066 | 0.0090 | 0.015 |
| Salivary glands | 0.0093 | 0.012 | 0.017 | 0.024 | 0.039 |
| Skin | 0.0018 | 0.0022 | 0.0035 | 0.0056 | 0.010 |
| Spleen | 0.0043 | 0.0054 | 0.0081 | 0.012 | 0.021 |
| Testes | 0.0028 | 0.0037 | 0.0058 | 0.0087 | 0.016 |
| Thymus | 0.0024 | 0.0032 | 0.0047 | 0.0075 | 0.014 |
| Thyroid | 0.022 | 0.036 | 0.055 | 0.12 | 0.22 |
| Uterus | 0.0081 | 0.010 | 0.015 | 0.022 | 0.037 |
| Other tissue | 0.0035 | 0.0043 | 0.0064 | 0.0096 | 0.017 |
| **Effective dose** **(mSv/MBq)** | **0.013** | **0.017** | **0.026** | **0.042** | **0.079** |

**(II) With pre-treatment with a blocking agent:**

|  |  |
| --- | --- |
| **Organ** | **Absorbed dose per administered unit activity (mGy/MBq) when blocking agents are administered** |
|  | **Adult** | **15 Year** | **10 Year** | **5 Year** | **1 Year** |
| Adrenals | 0.0029 | 0.0037 | 0.0056 | 0.0086 | 0.016 |
| Bladder wall | 0.030 | 0.038 | 0.048 | 0.050 | 0.091 |
| Bone surfaces | 0.0044 | 0.0054 | 0.0081 | 0.012 | 0.022 |
| Brain | 0.0020 | 0.0026 | 0.0042 | 0.0071 | 0.012 |
| Breast | 0.0017 | 0.0022 | 0.0032 | 0.0052 | 0.010 |
| Gallbladder | 0.0030 | 0.0042 | 0.0070 | 0.010 | 0.013 |
| Gastrointestinal tract |  |  |  |  |  |
| - Stomach wall | 0.0027 | 0.0036 | 0.0059 | 0.0086 | 0.015 |
| - Small intestine | 0.0035 | 0.0044 | 0.0067 | 0.010 | 0.018 |
| - Colon | 0.0036 | 0.0048 | 0.0071 | 0.010 | 0.018 |
| - Ascending colon wall | 0.0032 | 0.0043 | 0.0064 | 0.010 | 0.017 |
| - Descending colon wall | 0.0042 | 0.0054 | 0.0081 | 0.011 | 0.019 |
| Heart | 0.0027 | 0.0034 | 0.0052 | 0.0081 | 0.014 |
| Kidneys | 0.0044 | 0.0054 | 0.0077 | 0.011 | 0.019 |
| Liver | 0.0026 | 0.0034 | 0.0053 | 0.0082 | 0.015 |
| Lungs | 0.0023 | 0.0031 | 0.0046 | 0.0074 | 0.013 |
| Muscles | 0.0025 | 0.0031 | 0.0047 | 0.0072 | 0.013 |
| Oesophagus | 0.0024 | 0.0031 | 0.0046 | 0.0075 | 0.014 |
| Ovaries | 0.0043 | 0.0054 | 0.0078 | 0.011 | 0.019 |
| Pancreas | 0.0030 | 0.0039 | 0.0059 | 0.0093 | 0.016 |
| Red bone marrow | 0.0025 | 0.0032 | 0.0049 | 0.0072 | 0.013 |
| Skin | 0.0016 | 0.0020 | 0.0032 | 0.0052 | 0.0097 |
| Spleen | 0.0026 | 0.0034 | 0.0054 | 0.0083 | 0.015 |
| Testes | 0.0030 | 0.0040 | 0.0060 | 0.0087 | 0.016 |
| Thymus | 0.0024 | 0.0031 | 0.0046 | 0.0075 | 0.014 |
| Thyroid | 0.0024 | 0.0031 | 0.0050 | 0.0084 | 0.015 |
| Uterus | 0.0060 | 0.0073 | 0.011 | 0.014 | 0.023 |
| Other tissue | 0.0025 | 0.0031 | 0.0048 | 0.0073 | 0.013 |
| **Effective dose****(mSv/MBq)** | **0.0042** | **0.0054** | **0.0077** | **0.011** | **0.019** |

The effective dose resulting from the intravenous administration of 400 MBq of sodium pertechnetate (99mTc) to an adult weighing 70 kg is about 5.2 mSv.

After pretreatment of patients with a blocking agent and administration of 400 MBq of sodium pertechnetate(99mTc) to an adult weighing 70 kg the effective dose is about 1.7 mSv.

The radiation dose absorbed by the lens of the eye following administration of sodium pertechnetate(99mTc) for lacrimal duct scintigraphy is estimated to be 0.038 mGy/MBq. This results in an effective dose equivalent of less than 0.01 mSv for an administered activity of 4 MBq.

The specified radiation exposure is only applicable if all organs accumulating sodium pertechnetate (99mTc) will function normally. Hyper/hypofunction (e.g. of the thyroid, gastric mucosa or kidney) and extended processes with impairment to the blood-brain-barrier or renal elimination disorders, may result in changes to the radiation exposure, locally even in strong increases of it.

The surface dose rates and the accumulated dose depends on many factors. Overall, radiation measurements on the enviroment and during work are critical and should be practised.

**12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS**

Elution of the generator must be performed in premises complying with the national regulations concerning the safety of use of radioactive products.

The solution eluted is a clear and colourless sodium pertechnetate (99mTc) solution, with a pH between 4.0 and 8.0 and a radiochemical purity equal to or greater than 95% of the total radioactivity due to 99mTc.

When sodium pertechnetate (99mTc) solution is used for kit labelling, please refer to the package leaflet of the concerned kit.

Quality control

Radioactivity and the molybdenum (99Mo) break-through must be checked before administration.

The test for molybdenum (99Mo) break-through can be performed either according to Ph. Eur. or to any other validated methods able to determine a molybdenum (99Mo) content below 0.1 per cent of total radioactivity at the date and hour of administration.

The first eluate obtained from this generator can be normally used, unless otherwise specified.

Eluates even eluted later than 24 hours from the last elution can be used for kit labelling, unless it is excluded by the specifications of the relevant kit SmPC.

As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vials are compromised it should not be used.

Method of preparation

Radiopharmaceuticals should be prepared by the user in a manner, which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken complying with the requirements of Good Pharmaceutical Manufacturing Practice for radiopharmaceuticals.

**Instructions for elution of the Montek 10-40 GBq radionuclide generator.**

Safe handling

 Consideration should be given to the safe lifting and carrying of the generators. Local manual handling operations regulations should be observed in order to reduce the risk of injury caused by manual handling activities.

 Elution instructions

 The facilities used for elutions should comply with the appropriate regulations for safe radiological handling. Strict aseptic techniques should be used during the elution of the generator to ensure sterility of the generator eluate.

 To avoid unsatisfactory performance it is important to adhere to the following sequence of elution steps.

To elute the generator a vial of sodium chloride solution is placed onto the inlet needle. Elution of sodium pertechnetate (99mTc) solution, is achieved by placing a sterile evacuated vial onto the elution port.

**First elution**

1. Remove the generator and accompanying accessories from their packaging. Place the generator on a flat, level surface, in a suitably authorised and shielded location. **Do not remove** needle protector vials until you are ready to carry out the first elution.
2. Select a sodium chloride 9 mg/ml (0.9%) solution for injection vial containing the required volume of sodium chloride 9 mg/ml (0.9%) solution for injection.
3. Remove the flip-top from the sodium chloride 9 mg/ml (0.9%) solution for injection vial and swab the sodium chloride 9 mg/ml (0.9%) solution for injection vial closure using a supplied bactericidal swab and allow drying.
4. Remove the needle protector vial.
5. Place the sodium chloride 9 mg/ml (0.9%) solution for injection vial onto this needle, ensuring that it is fully pushed to the bottom of the inlet well.
6. Select an evacuated elution vial and swab the elution vial closure using a supplied bactericidal swab and allow drying. Prior to placing the elution vial inside the elution vial shield ensures that the vial contact surfaces of the shield have been swabbed using the bactericidal swab provided. **Do not remove** the elution needle protector vial until you are ready to place the elution vial on the needle.
7. Remove the needle protector vial and place the prepared shield containing elution vial on the needle. Please be sure needle hole on the elution vial shield fit the needle. Otherwise needle may be damaged or broken. Push down to ensure that the vial is fully located on the elution needle
8. You may realize air bubbles on the sodium chloride 9 mg/ml (0.9%) solution for injection vial and also you may realize the solution level in this vial is decreasing. Allow at least 3 minutes for the elution to proceed to completion. **Do not remove either the sodium chloride 9 mg/ml (0.9%) solution for injection vial or elution vial before the elution is complete.**
9. Slowly remove the elution vial shield to prevent damage to the elution needle.
10. Take the elution needle protector vial and push on to the elution needle to preserve sterility.
11. Leave the empty sodium chloride 9 mg/ml (0.9%) solution for injection vial in place until the next elution to preserve sterility.

Subsequent elution

Using a new sanitised sodium chloride 9 mg/ml (0.9 %) solution for injection vial of the required volume and an elution vial repeat steps 1–11.

**Elution activity and yield of technetium-99m**

 MONTEK 10-40 GBq radionuclide generator or is calibrated in terms of the amount of molybdenum loaded on the column. The available 99mTc at any time depends on the time before or after reference (due to the decay of 99Mo), the time elapsed since the previous elution (due to "growth" of 99mTc) and on the decay characteristics of 99Mo (86.2 % of all decay yields 99mTc). Factors listed in Tables 3 - 5 may be used to calculate the available 99mTc activity using the following method.

 First, multiply the stated reference activity by the appropriate factor from Table 3 (which allows for decay of 99Mo). Then multiply the product by the appropriate factor from Table 5 (which allows for the growth of 99mTc and for decay characteristics of 99Mo) or if you elute once you may use Table 6 directly if you elute the generator once a day. You may use Table 4 (which allows for decay of 99mTc) to calculate the eluate activity at any time.

 The actual yield of 99mTc will vary slightly due to variation in elution efficiency from generator to generator. It should typically be not less than 90% of the available 99mTc activity*.*

***Table 3 99Mo decay Table (99Mo half-life 66 hours)***

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *T (hours)* | *0* | *1* | *2* | *3* | *4* | *5* | *6* | *7* | *8* | *9* |
| *0*  | *1.0000*  | *0.9896*  | *0.9792*  | *0.9690*  | *0.9589*  | *0.9488*  | *0.9389*  | *0.9291*  | *0.9194*  | *0.9098*  |
| *10* | *0.9003*  | *0.8909*  | *0.8816*  | *0.8724*  | *0.8633*  | *0.8542*  | *0.8453*  | *0.8365*  | *0.8278*  | *0.8191* |
| *20* | *0.8105*  | *0.8021*  | *0.7937*  | *0.7854*  | *0.7772*  | *0.7691*  | *0.7610*  | *0.7531*  | *0.7452*  | *0.7374* |
| *30* | *0.7297*  | *0.7221*  | *0.7146*  | *0.7071*  | *0.6997*  | *0.6924*  | *0.6852*  | *0.6780*  | *0.6709*  | *0.6639* |
| *40* | *0.6570*  | *0.6501*  | *0.6433*  | *0.6366*  | *0.6300*  | *0.6234*  | *0.6169*  | *0.6104*  | *0.6040*  | *0.5977* |
| *50* | *0.5915*  | *0.5853*  | *0.5792*  | *0.5731*  | *0.5672*  | *0.5612*  | *0.5554*  | *0.5496*  | *0.5438*  | *0.5381* |
| *60* | *0.5325*  | *0.5270*  | *0.5215*  | *0.5160*  | *0.5106*  | *0.5053*  | *0.5000*  | *0.4948*  | *0.4896*  | *0.4845* |
| *70* | *0.4794*  | *0.4744*  | *0.4695*  | *0.4646*  | *0.4597*  | *0.4549*  | *0.4502*  | *0.4454*  | *0.4408*  | *0.4362* |
| *80* | *0.4316*  | *0.4271*  | *0.4227*  | *0.4182*  | *0.4139*  | *0.4096*  | *0.4053*  | *0.4010*  | *0.3968*  | *0.3927* |
| *90* | *0.3886*  | *0.3845*  | *0.3805*  | *0.3765*  | *0.3726*  | *0.3687*  | *0.3649*  | *0.3611*  | *0.3573*  | *0.3536* |
| *100* | *0.3499*  | *0.3462*  | *0.3426*  | *0.3390*  | *0.3355*  | *0.3320*  | *0.3285*  | *0.3251*  | *0.3217*  | *0.3183* |

***Table 4*** *99mTc* ***decay Table (****99mTc* ***half-life 6.01 hours)***

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Minutes**Hours* | *0* | *6* | *12* | *18* | *24* | *30* | *36* | *42* | *48* | *54* |
| *0* | *1.0000* | *0.9885* | *0.9772* | *0.9660* | *0.9549* | *0.9439* | *0.9331* | *0.9224* | *0.9118* | *0.9014* |
| *1* | *0.8910* | *0.8808* | *0.8707* | *0.8607* | *0.8508* | *0.8411* | *0.8314* | *0.8219* | *0.8124* | *0.8031* |
| *2* | *0.7939* | *0.7848* | *0.7758* | *0.7669* | *0.7581* | *0.7494* | *0.7408* | *0.7323* | *0.7239* | *0.7156* |
| *3* | *0.7074* | *0.6993* | *0.6913* | *0.6833* | *0.6755* | *0.6677* | *0.6601* | *0.6525* | *0.6450* | *0.6376* |
| *4* | *0.6303* | *0.6231* | *0.6159* | *0.6089* | *0.6019* | *0.5950* | *0.5881* | *0.5814* | *0.5747* | *0.5681* |
| *5* | *0.5616* | *0.5552* | *0.5488* | *0.5425* | *0.5363* | *0.5301* | *0.5240* | *0.5180* | *0.5121* | *0.5062* |
| *6* | *0.5004* | *0.4947* | *0.4890* | *0.4834* | *0.4778* | *0.4723* | *0.4669* | *0.4616* | *0.4563* | *0.4510* |
| *7* | *0.4459* | *0.4408* | *0.4357* | *0.4307* | *0.4258* | *0.4209* | *0.4160* | *0.4113* | *0.4066* | *0.4019* |
| *8* | *0.3973* | *0.3927* | *0.3882* | *0.3838* | *0.3794* | *0.3750* | *0.3707* | *0.3664* | *0.3622* | *0.3581* |
| *9* | *0.3540* | *0.3499* | *0.3459* | *0.3419* | *0.3380* | *0.3341* | *0.3303* | *0.3265* | *0.3228* | *0.3191* |
| *10* | *0.3154* | *0.3118* | *0.3882* | *0.3047* | *0.3012* | *0.2977* | *0.2943* | *0.2909* | *0.2876* | *0.2843* |
| *11* | *0.2810* | *0.2778* | *0.2746* | *0.2715* | *0.2684* | *0.2653* | *0.2622* | *0.2592* | *0.2562* | *0.2533* |
| *12* | *0.2504* | *0.2475* | *0.2447* | *0.2419* | *0.2391* | *0.2364* | *0.2337* | *0.2310* | *0.2283* | *0.2557* |

***Table 5 Factors allowing for growth of*** *99mTc* ***at various times following the previous elution***

***(****99mTc* ***half-life 6.01 hours)***

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***Hours*** | ***Factor*** | ***Hours*** | ***Factor*** | ***Hours*** | ***Factor*** | ***Hours*** | ***Factor*** | ***Hours*** | ***Factor*** | ***Hours*** | ***Factor*** |
| *1* | *0.094* | *9* | *0.579* | *17* | *0.788* | *25* | *0.879* | *33* | *0.918* | *41* | *0.935* |
| *2* | *0.179* | *10* | *0.615* | *18* | *0.804* | *26* | *0.884* | *34* | *0.921* | *42* | *0.937* |
| *3* | *0.256* | *11* | *0.648* | *19* | *0.818* | *27* | *0.892* | *35* | *0.924* | *43* | *0.938* |
| *4* | *0.324* | *12* | *0.678* | *20* | *0.831* | *28* | *0.898* | *36* | *0.926* | *44* | *0.940* |
| *5* | *0.386* | *13* | *0.705* | *21* | *0.843* | *29* | *0.903* | *37* | *0.929* | *45* | *0.941* |
| *6* | *0.442* | *14* | *0.729* | *22* | *0.853* | *30* | *0.907* | *38* | *0.930* | *46* | *0.941* |
| *7* | *0.492* | *15* | *0.751* | *23* | *0.863* | *31* | *0.911* | *39* | *0.932* | *47* | *0.941* |
| *8* | *0.538* | *16* | *0.771* | *24* | *0.871* | *32* | *0.915* | *40* | *0.934* | *48* | *0.942* |

***Table 6: TABLE of (99mTc) ACTIVITIES OBTAINED FROM MONTEK 10-40 GBq RADIONUCLIDE GENERATORS***

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***DAYS*** | ***MONTEK 10*** | ***MONTEK 15*** | ***MONTEK 20*** | ***MONTEK 25*** | ***MONTEK 30*** | ***MONTEK 35*** | ***MONTEK 40*** |
| ***mCi*** | ***MBq*** | ***mCi*** | ***MBq*** | ***mCi*** | ***MBq*** | ***mCi*** | ***MBq*** | ***mCi*** | ***MBq*** | ***mCi*** | ***MBq*** | ***mCi*** | ***MBq*** |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *-6* | *Friday* | *1,079* | *39,923* | *1,631* | *60,347* | *2,183* | *80,771* | *2,734* | *101,158* | *3,286* | *121,582* | *3,838* | *142,006* | *4,390* | *162,430* |
| *-5* | *Saturday* | *831* | *30,747* | *1,256* | *46,472* | *1,680* | *62,160* | *2,105* | *77,885* | *2,530* | *93,610* | *2,955* | *109,335* | *3,380* | *125,060* |
| *-4* | *Sunday* | *640* | *23,680* | *967* | *35,779* | *1,294* | *47,878* | *1,621* | *59,977* | *1,948* | *72,076* | *2,275* | *84,175* | *2,602* | *96,274* |
| *-3* | *Monday* | *492* | *18,204* | *744* | *27,528* | *996* | *36,852* | *1,248* | *46,176* | *1,500* | *55,500* | *1,752* | *64,824* | *2,004* | *74,148* |
| *-2* | *Tuesday* | *379* | *14,023* | *573* | *21,201* | *767* | *28,379* | *961* | *35,557* | *1,155* | *42,735* | *1,349* | *49,913* | *1,543* | *57,091* |
| *-1* | *Wednesday* | *292* | *10,804* | *441* | *16,317* | *590* | *21,830* | *740* | *27,380* | *889* | *32,893* | *1,038* | *38.406* | *1,188* | *43,956* |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ***0*** | ***Thursday*** | ***225*** | ***8,325*** | ***340*** | ***12,580*** | ***455*** | ***16,835*** | ***570*** | ***21,090*** | ***685*** | ***25,345*** | ***800*** | ***29,600*** | ***915*** | ***33,855*** |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *+1* | *Friday* | *173* | *6,401* | *261* | *9,657* | *350* | *12,950* | *438* | *16,206* | *527* | *19,499* | *616* | *22,792* | *704* | *26,048* |
| *+2* | *Saturday* | *133* | *4,921* | *201* | *7,437* | *269* | *9,953* | *337* | *12,469* | *406* | *15,022* | *474* | *17,538* | *542* | *20,054* |
| *+3* | *Sunday* | *102* | *3,774* | *155* | *5,735* | *207* | *7,659* | *260* | *9,620* | *312* | *11,544* | *365* | *13,505* | *417* | *15,429* |
| *+4* | *Monday* | *79* | *2,923* | *119* | *4,403* | *159* | *5,883* | *200* | *7,400* | *240* | *8,880* | *281* | *10,397* | *321* | *11,877* |
| *+5* | *Tuesday* | *60* | *2,220* | *92* | *3,404* | *123* | *4,551* | *154* | *5,698* | *185* | *6,845* | *216* | *7,992* | *247* | *9,139* |
| *+6* | *Wednesday* | *46* | *1,702* | *70* | *2,590* | *94* | *3,478* | *118* | *4,366* | *142* | *5,254* | *166* | *6,142* | *190* | *7,030* |
| *+7* | *Thursday* | *36* | *1,332* | *54* | *1,998* | *73* | *2,701* | *91* | *3.367* | *109* | *4,033* | *128* | *4,736* | *146* | *5,402* |
| *+8* | *Friday* |  *27* |  *999* | *42* | *1,554* | *56* | *2,072* | *70* | *2,590* | *84* | *3,108* | *98* | *3,626* | *113* | *4,181* |
| *+9* | *Saturday* | *21* | *777* | *32* | *1,184* | *43* | *1,591* | *54* | *1,998* | *65* | *2,405* | *76* | *2,812* | *87* | *3,219* |
| *+10* | *Sunday* | *16* | *592* | *24* | *888* | *33* | *1,221* | *41* | *1,517* | *50* | *1,850* | *58* | *2,146* | *67* | *2,479* |
| *+11* | *Monday* | *12* | *444* | *19* | *703* | *25* | *925* | *32* | *1,184* | *38* | *1,406* | *45* | *1,665* | *51* | *1,887* |
| *+12* | *Tuesday* | *9* | *333* | *14* | *518* | *19* | *703* | *24* | *888* | *29* | *1,073* | *34* | *1,258* | *39* | *1,443* |
| *+13* | *Wednesday* | *7* | *259* | *11* | *407* | *15* | *555* | *19* | *703* | *22* | *814* | *26* | *962* | *30* | *1,110* |
| *+14* | *Thursday* | *5* | *185* | *8* | *296* | *11* | *407* | *14* | *518* | *17* | *629* | *20* | *740* | *23* | *851* |
| *+15* | *Friday* | *4* | *148* | *6* | *222* | *9* | *333* | *11* | *407* | *13* | *481* | *15* | *555* | *18* | *666* |

*\*Elution Activity is the activity obtained from a generator eluted at 8 A.M* (GMT +3) *by at least 5 ml sodium chloride 9 mg/ml (0.9%) solution for injection that is not eluted during 24 hours.*

*\*\* The activities to be obtained are the 90-110% of the given activity amounts.*