General precautions
1. Collecting specimens from the pharynges with a pharyngeal swab is more effective than using a nasal swab or nasal aspirate, which have lower positive rates as they collect smaller amounts of virus.
2. The test plate should be used immediately after opening the packaging as it absorbs moisture and the quality deteriorates. Accurate results cannot be obtained.
3. Usage, dosage and instructions should be followed when using the kit.
4. A diagnosis should be made by a doctor based on an overall determination including not only the test result provided by this product, but also the results of other tests, viral isolation cultures, and clinical symptoms.
5. An Adenovirus is a highly contagious virus. Take appropriate steps to prevent in-hospital infection.
6. When collecting the pharyngeal swab, avoid touching saliva. If the specimen is mixed with saliva, the test result lines may become fainter on the test plate.
7. This reagent can be used for in-vitro diagnosis (IVD). Using the reagent for the purposes other than IVD are not permitted.
8. Please use this reagent following the operational method described in this package insert. We cannot guarantee results obtained by any operations used for any other purposes not described in the package insert.
9. Specimen extracts contain sodium azide. If the solution contacts eyes, mouth, or skin by mistake, take emergency measures. Wash thoroughly with water and receive medical treatment if necessary.

Kit components
Test plate
- Colloidal platinum-gold labeled anti-Adenovirus monoclonal antibody (mouse)
- Anti-Adenovirus monoclonal antibody (mouse)
Specimen extracts
- Buffer, detergent, sodium azide
Swab
Opener
Filter nozzle tip

Intended use
Detecting Adenovirus antigens by pharyngeal swab, nasal swab, nasal aspirate or keratoconjunctivitis swab (diagnostic assistance for Adenovirus infections).
**Test procedure principles**

This product consists of a test plate with a carrier strip composed of a sample placing area, a reagent area including a colloidal platinum-gold labeled anti-Adenovirus monoclonal antibody (mouse) (hereafter referred to as “colloidal platinum-gold labeled Adenovirus antibody”) and a developing area that fixes the anti-Adenovirus monoclonal antibody (mouse) (hereafter referred to as “anti-Adenovirus antibody”).

When a sample is placed on the sample placing area of the test plate, the colloidal platinum-gold labeled Adenovirus antibody dissolves and forms an immune complex with the Adenovirus antigens in the sample. This immune complex migrates through the developing area by capillary action, is captured by the anti-Adenovirus antibody fixed in the developing area. Colloidal platinum-gold forms a black line in the reading area [T]. The black line visually indicates the presence of Adenovirus antigens in the sample.

Regardless of the existence of Adenovirus antigens in the sample, excess colloidal platinum-gold labeled Adenovirus antibodies further migrate through the developing area, becoming captured by anti-mouse immunoglobulin antibody fixed in the reading area [C]. A black line forms in the reading area [C]. This means the colloidal platinum-gold labeled Adenovirus antibodies have migrated normally.

**Detection of Adenovirus antigen by the immunochromatography**

**Operational Precautions**

The collected specimen should be processed as soon as possible, according to the following procedure. All the specimens should be handled with extreme care, with all of them considered as they pose a risk of infection.
Interfering substances
Blood and the following OTC drugs or prescription drugs have no effect on the test results.
Whole blood (0.25%), three types of commercially available cold remedies (0.075~1.125%), three
types of commercially available cough drops (4%), two types of commercially available eye drops
(25%), two types of commercially available nasal drops (25%), two types of commercially available
gargles (25%), commercially available oral washing solutions (25%), acetylsalicylic acid (20mg/mL),
acetaminophen (10mg/mL), ibuprofen (11.25mg/mL), ambroxol hydrochloride (375mg/mL),
oxymetazoline hydrochloride (100ng/mL), oseltamivir (7.5mg/mL), L- carboxylic acid (12.5mg/mL),
disodium cromoglycate (5mg/mL), zanamivir (500ng/mL), salicylamide (6.75mg/mL), ciproheptadine
hydrochloride hydrate (200ng/mL), cefixime (2.5mg/mL), dextromethorphan hydrochloride (10mg/mL),
naphazoline nitrate (125ng/mL), nifedipine (1mg/mL), fluticasone propionate (127.5mg/mL),
chlorpheniramine maleate (5mg/mL), levofloxacin (2.5mg/mL), and loxoprofen sodium (3mg/mL).

Instructions for use
1. Methods of specimen collection
   1) Test plate
      Use as is.
   2) Specimen extracts
      Use as is.
2. Test preparation items
   1) Nasal swab: nasal sterile swab
      Nasal aspirate: suction machine, sucking trap
   2) Sample
      (1) Specimen collection methods
         ① Pharyngeal swab sampling
            Firmly insert the pharyngeal sterile swab (enclosed in kit) into the pharynx through the oral
cavity, and collect the mucosal cuticle by swabbing the posterior wall of the pharynx and the
palatine tonsil several times, centering around the reddening portion. Avoid touching
saliva. If the specimen is mixed with saliva, the test result lines may become fainter
on the test plate.
         ② Nasal swab sampling
            Firmly insert the sold separately swab into the nasal cavity and collect mucosal cuticle by
swabbing the nasal turbinate several times.
         ③ Nasal aspirate sampling
            Firmly insert one tube of the sucking trap into the suction pump, and the other tube into the
nasal cavity through an external nostril. Collect the nasal discharge aspirate in the sucking
trap by operating the suction pump.
            Soak the attached swab in the relatively low viscous portion of the nasal aspirate collected,
avoiding the highly viscous portion or solid portion.
         ④ Keratoconjunctivitis swab sampling
            Use attached sterile swab, and collect the cuticle by scratching hard the keratoconjunctivitis
several times. If necessary, use a surface anesthetic and scratch the area of inflammation
as strongly as you can.
(2) Sample preparation
Tear off the top seal of the extraction vial with the enclosed opener. Dip the swab into the specimen extract in the extraction vial immediately after specimen collection and stir. Pinch the head of the swab from outside of the extraction vial and draw out the swab while squeezing. Use the squeezed solution as the test sample.

(3) Sample preparation precautions
① If the sample is highly viscous that it clogs the filter, dilute the sample with the saline twofold (2x) before use.
② Using the nasal aspirate as it is for other test methods (e.g. isolation culture method, etc.)
③ If a part of the specimen is used for other test methods such as isolation culture, place 1 mL transport medium or saline in the tube in advance. Immediately after sampling specimen, insert the swab into the transport medium or saline in the tube and stir well. Use the portion of this solution for other test methods and dilute the remaining solution with the specimen extract twofold (2x) as in the test sample in this kit.

(4) Test procedure
① Firmly attach the filter nozzle to the top of the extraction vial.
② Hold the middle of the extraction vial with fingers and drop three drops of the sample (80 - 120 µL) into the sample placing area of the test plate. Hold the extraction vial perpendicularly and take care not to let the tip of the filter nozzle touch the sample placing area.
③ Observe the reading area of the test plate after 3 to 15-minutes and interpret the result.

Reading the result
1. Reading the result
Allow the samples to react according to the procedure and read the black lines that appear in the reading area. (The reading area must be viewed from directly overhead.)

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Positive" /></td>
<td><img src="image" alt="Negative" /></td>
</tr>
</tbody>
</table>

When black lines form at both [T] and [C] in the reading area (two lines), the result is read as positive. When a very faint black line is observed in the reading area [T], the result is also interpreted as positive.

When a black line is seen only at [C] in the reading area (one line), the result is interpreted as negative.

When a black line at [C] in the reading area is faint but visible, chromatographic development has occurred normally.

Retesting
When no black line is seen at [C] in the reading area, there may be some problem with the test procedure or the reagent quality. The test should be performed again, using another test plate. If the amount of antigens is very high, a very thick line may be observed at [T] in the reading area and no line may be absorbed at [C] in the reading area. In that case, dilute the sample with the specimen extract and perform the test again.

2. Interpreting test results precautions
Black lines observed both in the reading area [T] and [C] 3 to 15-minutes after sample placement are interpreted as positive. No black line in the reading area [T] even 15-minutes after sample placement indicates a negative result. Do not use the test plate for a reading result beyond the judgment time as
the result may change due to drying, etc.
A black line may not appear in the reading area [C] due to problems with the test plate procedure or
the reagent quality. In this case, the test should be performed again using another test plate. If the
same result is obtained in the re-test, try the test again using the sample diluted twofold (2x) with the
saline as the black line may not appear in the reading area [C] due to factors in the specimen or the
effects of saliva.
In the case of a very high antigen titer, a dense line may be seen in the reading area [T] and no black
line in the reading area [C]. In this case, dilute the sample with the specimen extract and repeat the
test. (e.g.) Dilutions sample method: apply three drops of a sample in a new extraction vial, mix
thoroughly and use the solution as the test sample.
The line is effective even if there is unevenness in depth and breaks in the line.
When discoloration is delayed due to some factor in the specimen or white discoloration is observed
on the line in the reading area [T], the phenomenon may be improved by extending the observation
time for an additional 5 minutes after a 15-minute wait.

**Performance**

1. **Performance**
   When sensitivity, specificity and reproducibility are tested according to usage and dosage described
above, using a positive control (1.0 - 1.5 x 10^4 viral particle/test), a weakly-positive control (1.0 – 1.5 x
10^3 viral particle/test), and a negative control (sample extract), the test results conform to the
following requirements.
   1) Sensitivity test
      When a positive control and a weakly-positive control are tested as samples, the result is positive.
   2) Specificity test
      When a positive control, a weakly-positive control, and a negative control are tested as samples,
      the results are positive for the positive control and the weakly-positive control, and negative for the
      negative control.
   3) Reproducibility test
      When a positive control, a weakly-positive control and a negative control are tested in triplicate,
      the results are all positive for the positive control and weakly-positive control, and all negative for
      the negative control.

2. **Minimum detection limit**
The minimum detection limit is 5 x 10^2 viral particle/test (using 100µL sample of 5 x 10^3 viral
particle/mL for one test).

3. **Correlation with a conventional test method**
   1) Pharyngeal swab

<table>
<thead>
<tr>
<th></th>
<th>Comparison product A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>ImunoAce Adeno</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
</tr>
</tbody>
</table>

Positive concordance rate: 100.0%
Negative concordance rate: 99.2%
Total concordance rate: 99.5%
(Note 1) Positive by PCR method.
<table>
<thead>
<tr>
<th>Comparison product B</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ImunoAce Adeno</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>52</td>
<td>5</td>
<td>57</td>
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<tr>
<td>Negative</td>
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<td>125</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>129</td>
<td>182</td>
</tr>
</tbody>
</table>

Positive concordance rate: 98.1%
Negative concordance rate: 96.1%
Total concordance rate: 98.7%

(Note 2) Negative by PCR method.
(Note 3) These five specimens are positive when tested by PCR method.

2) Nasal swab

<table>
<thead>
<tr>
<th>Comparison product A</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ImunoAce Adeno</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
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<td>56</td>
</tr>
<tr>
<td>Negative</td>
<td>2</td>
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<td>58</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>56</td>
<td>114</td>
</tr>
</tbody>
</table>

Positive concordance rate: 96.6%
Negative concordance rate: 100.0%
Total concordance rate: 98.2%

(Note 4) These two specimens are negative when tested by PCR method.

<table>
<thead>
<tr>
<th>PCR</th>
<th>Positive</th>
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<th>Total</th>
</tr>
</thead>
<tbody>
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<td>ImunoAce Adeno</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>55</td>
<td>1</td>
<td>56</td>
</tr>
<tr>
<td>Negative</td>
<td>2</td>
<td>56</td>
<td>58</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>57</td>
<td>114</td>
</tr>
</tbody>
</table>

Positive concordance rate: 96.5%
Negative concordance rate: 98.2%
Total concordance rate: 97.4%

3) Nasal aspirate

<table>
<thead>
<tr>
<th>Comparison product A</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ImunoAce Adeno</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>53</td>
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<td>53</td>
</tr>
<tr>
<td>Negative</td>
<td>5</td>
<td>54</td>
<td>59</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>54</td>
<td>112</td>
</tr>
</tbody>
</table>

Positive concordance rate: 91.4%
Negative concordance rate: 100.0%
Total concordance rate: 95.5%

(Note 5) These five specimens are negative when tested by PCR method.

<table>
<thead>
<tr>
<th>PCR</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ImunoAce Adeno</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>52</td>
<td>1</td>
<td>53</td>
</tr>
<tr>
<td>Negative</td>
<td>1</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>59</td>
<td>112</td>
</tr>
</tbody>
</table>

Positive concordance rate: 98.1%
Negative concordance rate: 98.3%
Total concordance rate: 98.2%

4) Keratoconjunctivitis swab

<table>
<thead>
<tr>
<th>Comparison product</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ImunoAce Adeno</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>61</td>
<td>3</td>
<td>64</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>133</td>
<td>133</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>136</td>
<td>197</td>
</tr>
</tbody>
</table>

Positive concordance rate: 100.0%
Negative concordance rate: 97.8%
Total concordance rate: 98.5%

(Note 6) Two of these specimens are positive; one specimen is negative when tested by PCR method.

<table>
<thead>
<tr>
<th>PCR</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>62</td>
<td>2</td>
<td>64</td>
</tr>
<tr>
<td>Negative</td>
<td>6</td>
<td>127</td>
<td>133</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>129</td>
<td>197</td>
</tr>
</tbody>
</table>

Positive concordance rate: 91.2%
Negative concordance rate: 98.4%
Total concordance rate: 95.9%
4. Reactive property with serological type
ImunoAce Adeno is responsive to Adenovirus type 1 - 8, 11, 19 and 37.

5. Cross-reactivity test result
No cross-reactivity was found in bacteria and viruses listed below.

1) Bacillus
   Acinetobacter baumannii
   Bacillus cereus
   Bacteroides fragilis
   Bordetella pertussis
   Branhamella catarrhalis
   Capnocytophaga ochracea
   Citrobacter freundii
   Enterobacter cloacae
   Enterococcus faecalis
   Eikenella corrodens
   Fusobacterium nucleatum
   Gardnerella vaginalis
   Haemophilus infuenzae
   Haemophilus parainfluenzae
   Kingella kingae
   Klebsiella oxytoca
   Lactobacillus casei
   Mycobacterium abscessus
   Mycobacterium avium
   Mycobacterium intracellulare
   Mycobacterium tuberculosis
   Neisseria meningitides
   Nocardia asteroids
   Pasteurella multocida
   Peptostreptococcus anaerobius
   Porphyromonas asaccharolyticus
   Prevotella intermedia
   Prevotella melaninogenica
   Salmonella choleraesuis (sub, Minnesota)
   Serratia marcescens
   Staphylococcus aureus
   Staphylococcus epidermidis
   Streptococcus bovis ( Ⅱ Group D)
   Streptococcus Group A
   Streptococcus Group B
   Streptococcus Group C
   Streptococcus Group F
   Streptococcus Group G
   Streptococcus milleri
   Streptococcus mutans
   Streptococcus oralis
   Streptococcus pneumoniae
   Streptococcus sanguis

2) Virus
   Influenza virus A (H1N1)
   Influenza virus A (H3N2)
   Influenza virus B
   Influenza virus C
   Parainfluenza virus Type 1
   Parainfluenza virus Type 2
   Parainfluenza virus Type 3
   Parainfluenza virus Type 4
   Respiratory syncytial virus (A)
   Respiratory syncytial virus (B)
   Rhinovirus Type 2
   Coxsackievirus Type A9
   Coxsackievirus Type A16
   Coxsackievirus Type B1
   Coxsackievirus Type B2
   Coxsackievirus Type B3
   Coxsackievirus Type B4
   Coxsackievirus Type B5
   Coxsackievirus Type B6
   Echovirus Type 4
   Echovirus Type 6
   Echovirus Type 9
   Echovirus Type 11
   Echovirus Type 14
   Echovirus Type 16
   Cytomegalovirus
   Human Metapneumovirus

3) Chlamydia
   Chlamydia pneumoniae
   Chlamydia psittaci
Handling precautions
1. Handling and hazard control precautions
   1) An Adenovirus is a highly contagious virus. There are some reports of in-hospital infection through healthcare personnel's hands and fingers, or medical devices. Even if the test result is negative, it does not mean there is no possibility of infection. Washing hands, sterilizing medical devices, and using gloves should be enforced to prevent in-hospital infection.
   2) If the specimen extract contacts the eyes, immediately flush with large quantities of water for 15 minutes or more. See a doctor if symptoms persist.
   3) If the specimen extracts contact hands or clothes, wash them with soap and large quantities of water.

2. Procedural precautions
   1) This product is a reagent intended to rapidly detect Adenovirus antigens. A definite diagnosis should be made by an attending physician in combination with clinical symptoms, results of the viral isolation culture, and other test results.
   2) Avoid touching saliva when collecting pharyngeal swab.
   3) Collecting specimens from the pharynges is preferable because nasal swabs or nasal aspirates have a lower positive rate with smaller amounts of virus when they are compared to a pharyngeal swab.
   4) Usage, dosage and instructions in the product insert should be followed when using the kit.
   5) In order to prevent deterioration, the product should be stored between 2 – 30°C, avoiding high temperatures, high humidity and direct sunlight.
   6) If the kit has been refrigerated, it must removed from the fridge at least thirty minutes before use and must be at room temperature when used for testing.
   7) The aluminum pouches containing test plates should not be opened until they are about to be used.
   8) The sample placing area or the reading area of the test plate should not be touched with hands.
   9) A precipitate may be seen in the specimen extract but the product can be used as it is since the precipitate is confirmed not to affect test results.
   10) Be sure to use enclosed filter nozzle.
   11) Do not use any reagents beyond the expiration date.

3. Disposal precautions
   1) Since test plates, swabs, extraction vials, filter nozzles, dropper tubes, remaining samples, etc. may cause infections, they should be autoclaved (121°C, 20 min) or soaked in 0.1 % hypochlorite for more than one hour. When reagents, remaining reagents, or their accessories are disposed of, they should be treated in accordance with the laws and regulations concerning medical waste disposal and water pollution control.
   2) The specimen extract contains 0.09% sodium azide as a preservative. When solutions containing sodium azide continues to be flushed down the drain over a long period of time, a metallic azide explosion may result if the drain is made of metal. Therefore, extract solutions should be discarded with large quantities of water.
**Storage, Validity**

Storage: store at 2 – 30°C
Validity: 18 months
An expiry date is on the outer box.

**Marketing Approval Holder in Japan**
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Fax: +81-55-925-6161