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<p>(21) International Application Number: PCT/GB89/00978 (22) International Filing Date: 23 August 1989 (23.08.89)</p> <p>(30) Priority data:</p> <table border="0"> <tr> <td>8820108.2</td> <td>24 August 1988 (24.08.88)</td> <td>GB</td> </tr> <tr> <td>8820945.7</td> <td>7 September 1988 (07.09.88)</td> <td>GB</td> </tr> <tr> <td>8911326.0</td> <td>17 May 1989 (17.05.89)</td> <td>GB</td> </tr> </table> <p>(71) Applicant (for all designated States except US): SMITH & NEPHEW PLC [GB/GB]; 2 Temple Place, Victoria Embankment, London WC2R 3BP (GB).</p> <p>(72) Inventor; and (75) Inventor/Applicant (for US only) : MILNER, Richard [GB/GB]; 3 Ashdale, Thorley Park, Bishops Stortford, Hertfordshire CM23 4EA (GB).</p> <p>(74) Agent: COLE, William, Gwyn; Smith & Nephew Research Ltd., Gilston Park, Harlow, Essex CM20 2RQ (GB).</p>		8820108.2	24 August 1988 (24.08.88)	GB	8820945.7	7 September 1988 (07.09.88)	GB	8911326.0	17 May 1989 (17.05.89)	GB	<p>(81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
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<p>(54) Title: ANTIMICROBIAL ARTICLES, THEIR PREPARATION AND USE</p> <p>(57) Abstract</p> <p>A method for the manufacture of an antimicrobial rubber article is described. The method comprises incorporating an effective amount of an antimicrobial agent into the natural rubber after the article has been shaped but before the article has been cured. Preferably the method comprises dipping the shaped article in its green state into an aqueous solution of an ionic antimicrobial agent such as chlorhexidine digluconate and then curing. Articles in the form of gloves are described. Gloves incorporating the antimicrobial agent may be used as surgeon's gloves or examination gloves.</p>											

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- 1 -

Antimicrobial Articles, their Preparation and Use.

This invention relates to antimicrobial articles and more particularly to gloves such as the type of gloves worn by medical practitioners such as surgeons, nurses and other medical or paramedical personnel, to their manufacture and to their use.

Conventionally surgical gloves are manufactured from extremely thin elastomeric materials such as natural or synthetic rubbers. These gloves fit closely and tightly over the users hand. One disadvantage which is experienced with this type of glove is that they are sometimes punctured or ruptured in use. The presence of any small hole such as that caused by a surgical needle or other surgical instrument can result in contamination and infection at the operation site by transfer of bacteria from the inside of the glove to the open wound or the surgical instruments. Also if body fluids of the patient carry viable bacteria or

viruses these may penetrate through a discontinuity in the glove and if they contact broken skin can cause infection of the surgical personnel involved. It has been suggested that channels can exist in latex gloves which allow viruses to pass through. Although it is the custom for the medical personnel to scrub their hands vigorously with an anti-infective skin cleanser before donning gloves, the anti-infective effect may be short lived and infective agents such as bacteria may regrow beneath the gloves in the moist warm environment. If a glove is punctured in use it may not be recognised and the operation is continued allowing risk of infection.

It has been suggested that a way of protecting the user of a glove is to provide a coating containing an anti-infective agent (see European Patent Publication No. 300814). A secure method of protection is required which does not rely upon maintaining the integrity of a coating both during manufacture and use. Such a method has now been discovered.

It has now been found that by immersing a coagulated but uncured glove shape formed from a natural rubber latex in a solution of an antimicrobial agent such as an aqueous solution of a water soluble ionic antimicrobial agent for example chlorhexidine digluconate, the antimicrobial agent is incorporated in

the latex without adverse effect thereto. The antimicrobial agent is dispersed throughout the glove material and is observed to release an antimicrobially effective amount of the antimicrobial agent from either surface of the glove. The risk of infection to the patient and glove wearer is reduced.

It is surprising that surface treatment of what will become the inner surface of the glove at this stage of its transformation into a glove yields a glove in which the antimicrobial agent is dispersed throughout the glove material. The antimicrobial agent is not restricted to a coating on the surface which becomes the inside of the glove. Microscopic examination of the inner and outer surface of the glove does not show evidence of a coating on either.

The level of antimicrobial agent available on the skin of the wearer is sufficient to inhibit many common bacteria and also to help to inhibit certain viruses. It is also believed that such a level would be sufficient to provide an improved barrier to infective agents including certain viruses such as the human immunosuppressive virus (H.I.V.).

An alternative way of coping with microbes was suggested in US Patent No. 4,675,347 in which it was

disclosed that although chlorhexidine salts caused gellation of natural rubber latices it was possible to use chlorhexidine salts in cationic latex. Unfortunately it is not always convenient or practicable to employ cationic latex in the manufacture of rubber articles and so it is desirable to have a process available which can use ordinary natural rubber latex.

The present invention is based on the discovery that the drawbacks of the above cited methods (that is the problem with having a layer as in said European Patent Specification or having to use cationic latex as in said US Patent Specification) can be avoided if an article made from natural rubber latex (ie non cationic) is treated with a antimicrobial agent such as chlorhexidine salt such as chlorhexidine digluconate in the "green state" or the "wet gel state", that is the state after the article has been formed but before it is cured.

The present invention provides a method for the manufacture of an antimicrobial rubber article which method comprises incorporating an effective amount of antimicrobial agent into the natural rubber latex after the article has been shaped but before the article has been cured.

This invention is most advantageous for the manufacture of gloves such as surgeon's gloves or examination gloves, but is also applicable to other rubber articles such as condoms, catheters such as urethral catheters, wound drains, endotracheal tubes, feeding tubes and the like. The benefits of the invention are most marked for thin walled articles such as gloves and condoms where improved barrier properties are particularly desired especially in view of the increasing occurrence of virus diseases such as those resulting from infection by human immunosuppressive virus.

A shaped but not yet cured rubber article is one which has taken up the desired configuration (for example by dipping a former of the desired configuration into the latex) and which is no longer water dispersible. A cured article is one which has dried and is normally fully vulcanised.

Rubber articles can be formed by dipping process which employ a coagulant and by processes which do not employ a coagulant. However, the method of this invention is particularly suitable for the manufacture of rubber articles by a process which employs a coagulant because problems with washing off

insufficiently gelled latex from the former when the antimicrobial agent is being introduced are effectively avoided.

Thus in a favoured aspect the present invention provides a method for the manufacture of an antimicrobial rubber article which method comprises incorporating an effective amount of an antimicrobial agent into the natural rubber latex after the article has been formed by dipping a coagulant coated former into natural rubber latex but before the article has been cured.

This version of the method of the invention is most suitably employed in the manufacture of gloves such as surgeon's gloves and examination gloves.

In the process of this invention it is desirable to incorporate a leaching step between the forming of the article and the incorporation of the antimicrobial agent. Thus in a preferred aspect this invention provides a method of manufacture of an antimicrobial rubber glove which includes the step of incorporating an antimicrobial agent into the natural rubber latex between the leaching and curing step in the glove forming process.

The incorporation of the antimicrobial agent is best achieved by dipping the green stage latex coated former into a solution of the antimicrobial in water. This is most aptly done at ambient temperatures for example at 20°C.

The manufacture of the gloves may be initiated as is conventional in the art by forming a coating of a coagulant on a heated glove shaped former. The coated former is then dipped into a natural rubber latex, withdrawn and then dipped into a warm water leach bath. After removal from the leach bath, the glove shape is dipped into a solution of an antimicrobial agent. After dipping the glove-shape is cured. Then it may be coated with a lubricating donning powder and stripped from the former. By being able to apply an antimicrobial agent in this way more complex processes of forming medicated rubber articles such as gloves are avoided. These complex processes include those processes which require swelling and deswelling the finished article with solvents in the presence of an active agent or which require the preparation of special medicated dusting powders or which provide coatings of the antimicrobial agent with special bonding agents.

The present invention also provides an antimicrobial glove which has incorporated in it an

antimicrobial agent using the process hereinbefore described.

The antimicrobial agent can be a water soluble antimicrobial agent and is preferably an ionic antimicrobial agent. Suitably the antimicrobial agent can have a solubility in water of greater than 0.1g/100g of water and more suitably greater than 1.0g/100g and preferably greater than 10g/100g of water (the solubilities may be measured at ambient temperatures, for example 20°C). Suitable antimicrobial agents include quaternary ammonium antimicrobial agents and chlorhexidine salts especially chlorhexidine digluconate and chlorhexidine diacetate of which chlorhexidine digluconate is preferred.

Accordingly the present invention provides a glove which has at least a portion of the inner surface thereof surface (ie. the wearer facing side) treated with chlorhexidine digluconate.

It is clear from the above that surface treatment during the glove forming process of the surface which becomes the inner surface of the glove with chlorhexidine digluconate solution results, after curing, in an antimicrobial natural rubber latex glove. The glove has incorporated throughout it chlorhexidine

digluconate. The glove is stable on storage. This is surprisingly advantageous since instability in natural rubber latex is observed if, for example a multivalent ionic material such as chlorhexidine digluconate is mixed with it. It is particularly surprising that the chlorhexidine digluconate does not simply remain on the treated surface but finds its way into the bulk of the rubber.

Accordingly in another aspect the present invention provides an antimicrobial rubber glove in which is incorporated throughout an antimicrobially effective amount of chlorhexidine digluconate.

It is very surprising that chlorhexidine digluconate is suitable for incorporating in a glove since it is a hygroscopic or even deliquescent solid and is usually only available as a solution. The treated gloves retain their antimicrobial properties and are stable on storage. The chlorhexidine digluconate appears not to effect any lubricating powder present by, for example, absorbing moisture onto the inner surface of the glove.

In a preferred aspect of the invention an antimicrobial glove formed by the process may contain a second antimicrobial agent. Aptly this second agent

will be incorporated in the glove material when in the form of the natural rubber latex. Suitable antimicrobial agents include non-ionic, sparingly water soluble antimicrobial agents for example halogenated hydroxy diphenyl derivatives such as 2,4,4'-trichloro-2'-hydroxy diphenyl ether (triclosan).

Aptly the halogenated hydroxy diphenyl derivative is a diphenyl ether. A particularly suitable diphenyl ether is 2,4,4'-trichloro-2'-hydroxy diphenyl ether (triclosan).

In another aspect the present invention provides an antimicrobial glove which contains a halogenated hydroxy phenyl derivative and a chlorhexidine salt.

In a further aspect the invention provides a glove which contains a halogenated hydroxy diphenyl derivative and is surface treated on at least a portion of its inner surface with chlorhexidine digluconate.

Such derivatives may be mixed with the glove material prior to forming the glove-shape. Suitably the glove material will contain an antimicrobially effective amount of the derivative. Suitably the glove material may contain from 0.1 to 10% w/w of the derivative, more suitably 0.5 to 5% w/w and preferably

1 to 4% w/w, for example, 1%, 2% 3% and 4%.

The gloves may be used as surgeon's gloves, as examination gloves or for any other purpose which it is desired to reduce the risk of infection. Aptly the glove is a surgeon's glove. Aptly the glove is an examination glove.

The antimicrobial agent such as chlorhexidine digluconate may be applied to the glove by dipping the glove-shape when on its former into an appropriate strength solution of the antimicrobial agent. Suitably the solution may contain from 0.05 to 25% by weight and more suitably from 0.1 to 10% by weight, for example 0.1%, 2%, 4%. These figures are particularly suitable for chlorhexidine digluconate. The amount of time the glove material spends in the solution depends upon the strength of the solution and the amount of the antimicrobial agent required in the glove. Typically a 1 or 2 minute dip in a 4% w/w aqueous solution chlorhexidine digluconate incorporates sufficient of the antimicrobial agent into the glove material, that is 3% w/w from a 1 minute dip and 4% w/w from a 2 minute dip.

The amount of antimicrobial agent incorporated in the glove by dipping process can be from 0.1 to 10% by

weight, more suitably can be 0.5 to 8% and is preferably 1 to 6%, for example 2 to 4%.

The use of a natural rubber latex to form the glove material is preferred. The use of this process to incorporate chlorhexidine salts in a natural rubber latex glove offers a method of overcoming many of the potential problems which could occur with natural rubber latex gloves if they are susceptible to penetration by viruses such as those responsible for AIDS and Hepatitis B.

It will be understood that in a preferred aspect this invention provides a thin rubber glove which contains chlorhexidine salt such as chlorhexidine digluconate. Such gloves offer the user a high degree of protection from common infecting organisms that might penetrate through any discontinuity in the glove. The use of such gloves can reduce the need for extensive pre-sterilisation of the skin as the antibacterial agent is effective in reducing skin flora especially after wet glove donning.

The present invention provides a method of reducing the risk of infection which comprises using thin polymer gloves which have incorporated therein by surface treatment thereof an antimicrobially effective

amount of chlorhexidine digluconate. Most aptly the gloves are donned onto wet (or at least damp) hands.

The use of a glove which has incorporated in it chlorhexidine digluconate and which also contains triclosan provides antimicrobial protection for the wearer for an extended period, for example upto 6 to 8 hours.

In a further aspect this invention provides a method of reducing the risk of infection which comprises using at least two pairs of thin rubber gloves which each contain an antimicrobial agent such as a chlorhexidine salt such as chlorhexidine digluconate.

In these further aspects of the invention the glove material may contain a second antibacterial agent as hereinbefore described.

The gloves of the present invention may be prepared by taking a glove former, heating it and dipping into a conventional coagulant solution. The former is removed and air-dried. The coated former is then immersed in a solution of the glove material. Preferably this is a pre-vulcanised natural rubber latex for example, 42% solids, aqueous dispersion and

optionally containing a second antibacterial agent. The coated former is then withdrawn, air-dried for about 2 minutes and immersed in a leach tank of warm water, at about 70°C, for about 2 minutes to extract any water soluble material. The former is removed and then immersed in an aqueous solution containing an appropriate concentration of the antimicrobial agent such as chlorhexidine digluconate. The glove-shape may be immersed for a period of between 10 seconds and 5 minutes, and more suitably 30 seconds to 4 minutes, depending on the strength of the solution. The glove is 'cured' in an oven, and may be dusted with lubricating powder before it is stripped from the former, everting the glove so that the antimicrobial surface treated surface forms the inner surface of the glove.

In a further preferred aspect therefore the present invention provides a method of making a glove which method comprises forming a coating of the glove material on a glove-shaped former, immersing the former in a solution of chlorhexidine digluconate, withdrawing it from the solution, optionally curing the glove material, optionally dusting the glove-shape with lubricating powder, stripping the glove from the former, thereby everting the glove so that the chlorhexidine digluconate treated surface forms the inner surface of the glove.

Preferably the glove material comprises a natural rubber. The coating on the former is obtained by dipping the former in a latex of pre-vulcanised natural rubber.

In a further aspect the invention represents an improvement in the method of manufacture of an antimicrobial rubber latex glove by (a) forming a dry coating of coagulant on a glove shaped former, (b) immersing the coated former in natural rubber latex, (c) leaching the coagulated latex in water, (d) curing the leached, coagulated latex to form the glove, the improvement comprising dipping the leached coagulated latex into a solution of an antimicrobial agent between the leaching and curing steps in the glove forming process. In this process the leaching step may be carried out at the same time as incorporating the antimicrobial agent (ie. the solution of the antimicrobial agent may be the leach bath) if desired.

Analogous methods to those hereinbefore described can be employed to prepare other shaped rubber articles.

Example 1Preparation of a Glove

A glove-shape was prepared in a conventional manner by coagulating a rubber latex on to a glove-shaped former and then leaching in a tank of warm water at 70°C for two minutes. After leaching the former was dipped in an aqueous solution containing 10% w/w of chlorhexidine digluconate for 20 seconds and then removed and shaken to remove adhering water droplets. The glove-shape was cured by placing in an oven at 115°C for 25 minutes, cooled, dusted with cross-linked cornstarch and stripped from the former causing the glove-shape to evert.

A sample of glove material prepared by the method described in Example 1 which had been immersed in various concentrations of chlorhexidine digluconate was placed with the treated surface contacting the surface of an agar growing medium seeded with *Staphylococcus aureus*. The plate was incubated and a zone of inhibition of growth of the bacteria around the samples was observed indicating successful release of the antibacterial agent. The results are shown in the following table:

<u>Percentage of Chlorhexidine Digluconate in Dip Solution</u>	<u>zone of Inhibition (mm)</u>
0 (control)	0.74
1	3.54
5	5.35
10	6.33

Example 2

Preparation of a Glove

A glove-shape was prepared in a similar manner to Example 1 except that the rubber latex contained 1% approx. by weight of triclosan. Triclosan is incorporated into the rubber latex by mixing the triclosan (21g) with a small quantity of latex to form a paste. The paste is gradually diluted with more latex (4870g) until the required concentration is achieved. The glove material after coagulation and leaching was dipped in a 4% aqueous solution of chlorhexidine digluconate for 1 minute and then cured. A sample of this antimicrobial glove material was tested in a similar manner to that described in Example 1 and gave a zone of inhibition of 5.64mm.

Example 3Preparation of a Glove

A dispersion of triclosan in water (at 40% solids) was formed by ball milling for 5 hours the following mixture:

Triclosan	100g
DARVAN No.1*	20g
Ammonium Caseinate (10% soln.)	20g
Water	to 250g

* sodium salts of polymerised alkylnaphthalene sulphonic acid (25% solution)

This dispersion was mixed with an aqueous rubber latex (solids content 41.5%) in the following proportions:

40% Triclosan dispersion	8.3g
Latex	to 800g

The two components were mixed until a homogenous mixture was achieved.

A glove was then prepared from the rubber latex incorporating triclosan by a similar method to that

described in Example 1 so that the finished glove contains both chlorhexidine digluconate and triclosan.

CLAIMS

1. A method for the manufacture of an antimicrobial rubber article which method comprises incorporating an effective amount of an antimicrobial agent into natural rubber latex after the article has been shaped but before the article has been cured.
2. A method for the manufacture of an antimicrobial rubber glove, including the step of incorporating an effective amount of an antimicrobial agent into the natural rubber latex between the leaching and curing step in the glove forming process.
3. A method as claimed in claim 1 including the step of dipping a glove shape of uncured natural rubber latex into a solution of an antimicrobial agent.
4. A method as claimed in claim 2 in which the glove shape is dipped into an aqueous solution of an ionic antimicrobial agent.
5. A method as claimed in claim 4 in which the aqueous solution contains from 0.1 to 10% by weight of chlorhexidine digluconate.

6. A method as claimed in any one of claims 1 to 5 in which the natural rubber latex has incorporated in it a non-ionic, sparingly water soluble antimicrobial agent.

7. A method as claimed in claim 6 in which the natural rubber latex incorporates from 0.1 to 10% of 2,4,4¹-trichloro-2¹-hydroxydiphenyl ether.

8. A rubber glove which has at least a portion of the inner surface thereof surface treated with chlorhexidine digluconate.

9. A rubber glove in which is incorporated throughout an antimicrobially effective amount of chlorhexidine digluconate.

10. An antimicrobial rubber glove, which has incorporated in it an effective amount of an antimicrobial agent by surface treating a natural rubber latex with the antimicrobial agent between the leaching and curing step in the glove forming process.

11. A glove as claimed in any one of claims 8 to 10 in which the surface treatment comprises dipping a glove shape of uncured natural rubber latex into a solution of the antimicrobial agent.

12. A glove as claimed in claim 10 in which the antimicrobial agent is a water soluble ionic antimicrobial agent.
13. A glove as claimed in claim 12 in which the antimicrobial agent is chlorhexidine digluconate.
14. A glove as claimed in any one of claims 8 to 10 in which the glove has incorporated in it from 0.5 to 8% of the antimicrobial agent.
15. A glove as claimed in any one of claims 8 to 10 in which the glove has also incorporated in it from 0.1 to 10% of a second antimicrobial agent which is a non-ionic, sparingly water soluble antimicrobial agent.
16. A glove according to claim 15 in which the second antimicrobial agent is 2,4,4¹-trichloro-2¹-hydroxy diphenyl ether.
17. A method of reducing the risk of infection which comprises using a natural rubber latex gloves which has incorporated therein an antimicrobially effective amount of chlorhexidine digluconate.

18. In a method of manufacturing an antimicrobial rubber latex glove by:

(a) forming a dry coating of coagulant on a glove shaped former,

(b) immersing the coated former in natural rubber latex,

(c) leaching the coagulated latex in water,

(d) curing the leached, coagulated latex to form the glove,

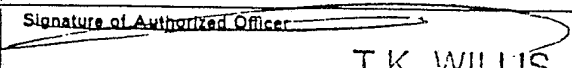
the improvement comprising dipping the leached coagulated latex into a solution of an antimicrobial agent between the leaching and curing steps in the glove forming process.

19. In a method as claimed in claim 18 the improvement wherein the leach bath contains the antimicrobial.

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 89/00978

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC ⁵ : A 61 L 31/00, A 61 B 19/04		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC ⁵	A 61 L, C 08 J, C 08 K, A 61 B	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched *		
III. DOCUMENTS CONSIDERED TO BE RELEVANT *		
Category ⁸	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	EP, A, 0229862 (TERUMO) 29 July 1987, see claims; page 3, lines 18-25; page 4, lines 1,2	
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A	EP, A, 0141628 (UNITIKA) 15 May 1985, see page 6, lines 16-22; claims & US, A, 4675347 (cited in the application)	
	--	
A	WO, A, 8605391 (B. GLUCK) 25 September 1986	
	--	
A	FR, A, 2215506 (JAMES NORTH & SONS LTD) 23 August 1974, see page 2, lines 19,20,26-39	

<p>* Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
28th November 1989	10. 01. 90	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	 T.K. WILLIS	

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.

GB 8900978
SA 30886

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 02/01/90. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0229862	29-07-87	AU-B- 558588	05-02-87
		JP-A- 61037248	22-02-86
EP-A- 0141628	15-05-85	JP-A- 60094460	27-05-85
		JP-A- 60096258	29-05-85
		US-A- 4675347	23-06-87
WO-A- 8605391	25-09-86	AU-B- 586243	06-07-89
		AU-A- 5660686	13-10-86
		EP-A- 0215072	25-03-87
		JP-T- 62502309	10-09-87
FR-A- 2215506	23-08-74	DE-A- 2302893	01-08-74