Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER:	(cwf)
FOLDER:	K020659 - 117 pages
COMPANY:	SSL AMERICAS, INC. (SSLAMER)
PRODUCT:	CONDOM (HIS)
SUMMARY:	Product: DUREX LATEX CONDOM WITH MALE GENITAL DESENSITIZER LUBRICANT
DATE REQUESTED:	Feb 8, 2016
DATE PRINTED:	Feb 8, 2016

Note: Printed

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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MAR 2 9 2002

PART VIII. 510(K) SUMMARY

Submitter by: SSL Americas, Inc.
3585 Engineering Drive
Norcross, Georgia 30092

Contact Person: Joyce Ning
Vice President, Regulatory Affairs
Phone: (770) 582-2152

Date Prepared: February 15, 2002

Proprietary Name: Durex® latex condom with male desensitizer lubricant

Common Name: Latex Condom

Classification Name: Condom (21 CFR § 884.5300)

Predicate Device: DUREX® Hispano Ico Latex Condom (K952415) and Male Condom with Desensitizer (K822088)

Description of the Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant is made of a natural rubber latex sheath with lubricant containing Benzocaine, an over-the-counter drug recognized as safe and effective by US FDA under 21 CFR 5300 for condom and 21 CFR Part 348 for external analgesic drug products for over-the-counter human use. The condom is a straight-walled, nipple-end condom with the nominal length of 180 mm and width of 52 mm as required by ASTM D-3492-97.

Intended Use of the Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant has the same intended use as the predicate condom. It is used for contraception and for prophylactic purposes to help reduce the risk of pregnancy and the transmission of sexually transmitted diseases (STDs). In addition, the male genital desensitizer lubricant on the condom helps in temporarily prolonging the time till ejaculation.

Technological Characteristics: Both the proposed device and the predicate device are of the similar design meeting ASTM Standard (D3492) specification for Rubber Contraceptives (Male Condoms). Both are straight-walled, nipple-end, lubricated made with the similar formulation of natural rubber latex. The proposed condom is a modification of the predicate device with variation merely in the lubricant application.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Joyce Ning
Vice President Regulatory Affairs
SSL Americas, Inc.
3585 Engineering Drive, Suite 200
P.O. Box 926090
NORCROSS GA 30092-9214

MAR 2 9 2002

Re: K020659
Trade Name/Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant
Regulation Number: 21 CFR 884.5300
Regulation Name: Condom
Regulatory Class: II
Product Code: 85 HIS
Dated: February 28, 2002
Received: March 1, 2002

Dear Ms. Ning:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

Please be advised that, as of March 25, 1998, labeling for latex condoms (21 CFR §884.5300 and §884.5310) must comply with Use Labeling for Latex Condoms: Expiration Dating, 21 CFR 801.435. Therefore, an expiration date, supported by test data developed under the conditions specified in §801.435(d), must be displayed prominently and legibly on condom labeling. For condoms with spermicidal lubricant, the effective shelf life of the spermicide must be compared with the shelf life of the condom and labeled with the earlier of the two expiration dates. Although supporting data is not to be provided in your 510(k) submission, §801.435(j) requires that you maintain this data and that it be available for inspection by FDA. Furthermore, §801.435(e) requires that if your real-time test data fails to confirm the shelf life estimated by the methods in §801.435(d), then you must relabel all product to reflect the actual shelf life. Condoms are not to be labeled with an expiration date that gives a shelf life more than five years.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (301) 594-4616. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR §807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597,or at its Internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Nancy C Brogdon

Nancy C. Brogdon
Director, Division of Reproductive, Abdominal,
and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART V. INDICATIONS FOR USE STATEMENT

3.0

Indications for Use Statement

Applicant: SSL-Americas, Inc.

510(k) Number (if known):* K020659

Device Name: DUREX® Latex Condom with Male Genital Desensitizer Lubricant

Indications for Use:

The DUREX® Latex Condom with Male Genital Desensitizer Lubricant is used for contraception and for prophylactic purposes to help reduce the risk of pregnancy and the transmission of sexually transmitted diseases. The male genital desensitizer lubricant on the condom helps in temporarily prolonging the time until ejaculation.

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use _____ **or** **Over-The-Counter Use** ✓

Nancy C. Brogdon
(Division Sign-Off)
Division of Reproductive, Abdominal, and Radiological Devices
510(k) Number K020659

Questions? Contact FDA/CDRH/OSEL/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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DEPARTMENT OF HEALTH & HUMAN SERVICES

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Ms. Joyce Ning
Vice President Regulatory Affairs
SSL Americas, Inc.
3585 Engineering Drive, Suite 200
P.O. Box 926090
NORCROSS GA 30092-9214

MAR 2 9 2002

Re: K020659
Trade Name/Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant
Regulation Number: 21 CFR 884.5300
Regulation Name: Condom
Regulatory Class: II
Product Code: 85 HIS
Dated: February 28, 2002
Received: March 1, 2002

Dear Ms. Ning:

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Sincerely yours,

Nancy C Brogdon

Nancy C. Brogdon
Director, Division of Reproductive, Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART V. INDICATIONS FOR USE STATEMENT

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Applicant: SSL-Americas, Inc.

510(k) Number (if known):* K020659

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use _____ **or** **Over-The-Counter Use** ✓

Nancy C. Brogdon
(Division Sign-Off)
Division of Reproductive, Abdominal, and Radiological Devices
510(k) Number K020659

Questions? Contact FOIA@CDRH-FOIA@fda.hhs.gov or 301-796-8118

3

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Ms. Joyce Ning
Vice President Regulatory Affairs
SSL Americas, Inc.
3585 Engineering Drive, Suite 200
P.O. Box 926090
NORCROSS GA 30092-9214

Re: K020659
Trade Name/Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant
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Sincerely yours,

Nancy C. Brogdon
Director, Division of Reproductive, Abdominal,
and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

cc: HFZ-401
HFZ-404
HFZ-470
D.O.

FILE COPY

Final: kjh 3/29/02

OFFICE	SURNAME	DATE		OFFICE	SURNAME	DATE		OFFICE	SURNAME	DATE
Z-470	Kuczewski	3/29/02								
Z-470	Pollard	3/29/02								
Z-470	Brogdon	3-29-02								

U.S. GPO 1986-169-089

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

From: Reviewer(s) - Name(s) Kucmiński (HFZ-470)

Subject: 510(k) Number K020659

To: The Record - It is my recommendation that the subject 510(k) Notification:

- ☐ Refused to accept.
- ☐ Requires additional information (other than refuse to accept).
- ☒ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.
  - De Novo Classification Candidate? ~~☐ YES ☐ NO~~ N/A
- ☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Postmarket Surveillance?	☐ YES	☒ NO
Is this device subject to the Tracking Regulation?	☐ YES	☒ NO
Was clinical data necessary to support the review of this 510(k)?	☐ YES	☒ NO
Is this a prescription device?	☐ YES	☒ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☒ NO
Special 510(k)?	☒ YES	☐ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☐ YES	☒ NO

This 510(k) contains:

Truthful and Accurate Statement ☐ Requested ☒ Enclosed
(required for originals received 3-14-95 and after)

☒ A 510(k) summary OR ☐ A 510(k) statement

☐ The required certification and summary for class III devices N/A

☒ The indication for use form (required for originals received 1-1-96 and after)

Material of Biological Origin ☐ YES ☒ NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 days

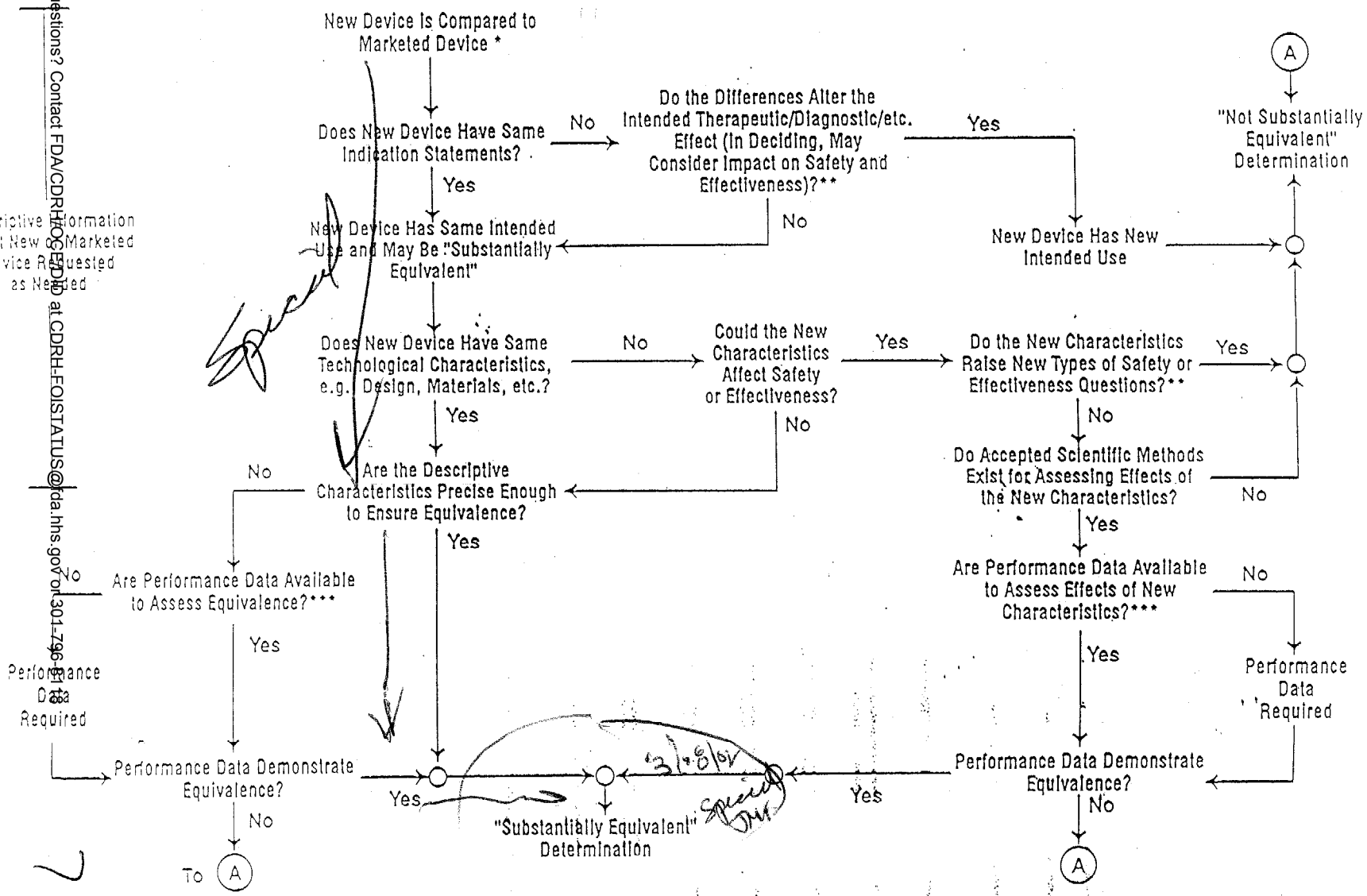
Predicate Product Code with class: Additional Product Code(s) with panel (optional):

21 CFR, §884.5300, Class II, 85 HIS

Review: Colin M Pollard (Branch Chief) OG DB (Branch Code) 3/29/02 (Date) JME

Final Review: Nancy C Brogdon (Division Director) 3-29-02 (Date)

510(k) "Substantial Equivalence" Decision-Making Process (Detailed)



* 510(k) Submissions Compare New Devices to Marketed Devices. FDA Requests Additional Information (Pre-Amendment... Relationship Between Marketed and "Predicate" ...ified Post-Amendments) Devices Is Unclear.

** This Decision Is Normally Based on Descriptive Information Alone, But Limited Testing Is Sometimes Required.

*** Data May Be ... 510(k), Other 510(k)s, The Center's Classification Files, or the Literature.

Questions? Contact FDA/CDRH/OSE/DSD at CDRH-FOISTATUS@fda.hhs.gov or 301-796-[illegible]

Descriptive Information ... Marketed Device Requested as Needed

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K020659 **OGDB**

SPECIAL 510(k): Device Modification
ODE Review Memorandum

SSL-AMERICAS, INC.
DUREX® LATEX CONDOM WITH MALE GENITAL DESENSITIZER LUBRICANT

Reviewer: J. Michael Kuchinski
Microbiologist

Division/Branch: DRAERD/ADOU/OGDB (HFZ-470)

Applicant: SSL Americas, Inc.
3585 Engineering Drive, Suite 200
P.O. Box 926090
Norcross, Georgia 30092-9214

Contact: Joyce Ning
Vice President, Regulatory Affairs
Phone: 770-582-2152
Facsimile: 770-582-2204

Trade Name: **Durex® Latex Condom with Male Genital Desensitizer Lubricant**

Common/Classification Name: Condom: 85 HIS, Class II, §884.5300

Product comparison: This is a special 510(k) submission in which SSL-Americas, Inc. is claiming that this device is a modification of currently marketed Durex® Latex Condoms manufactured by Hispano Ico Latex. Specifically, the condom subject to 510(k) K952415 and the Desensitizing Lubricated Male Condom (Schmid Laboratories) Latex condom with Male Desensitizing lubricant (K822088).

NARRATIVE DEVICE DESCRIPTION

Intended Use

Provide a brief description of the clinical purpose of this device, including indication(s) for use and any relevant promotional claims.

"The DUREX® Latex Condom with Male Genital Desensitizer Lubricant is used for contraception and for prophylactic purposes to help reduce the risk of pregnancy and the transmission of sexually transmitted diseases. The male genital desensitize lubricant on the condom helps in temporarily prolonging the time until ejaculation."

	Yes	No
Is the device life-supporting or life sustaining?		☑
Is the device implanted (short-term or long-term)?		☑
Does the device design use software?		☑
Is the device sterile?		☑
Is the device single use?	☑	
Is the device home use?	☑	
Is the device for prescription?		☑
Does the device contain a drug or biological Product as a component?	☑ spermicidal lubricant	
Is this device a kit?		☑

The remainder of this review follows the Special 510(K) Review Memorandum (revised:3/27/98)

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own **Class II** device requiring 510(k). The following items are present and acceptable:

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.
   Durex® Hispano Ico Latex Condom (K952415)
   Desensitized Male Condom (K822088)

   Examples of other condoms that include male desensitizing lubricants are:
   - Carter-Wallace - Trojan® Latex Condom with Male Desensitizer Lubricant (K000748)
   - P.T. Vonix Latexindo - Simplex Brand Male Latex Condoms (Silicone-lubricated with 4% Benzocaine Gel) (K011391)

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials.

   The application includes the submitter's statement that the 510(k) condom has the same intended use as the predicate condom. As stated, "The condom is used for contraception and for prophylactic purposes (to help reduce the risk of pregnancy and the transmission of sexually transmitted diseases, STDs)."

   The indication for use statement has been modified to include a statement: "The male genital desensitize lubricant on the condom helps in temporarily prolonging the time until ejaculation."
   This constitutes a change in the indication but is viewed as a minor change in the intended use, primarily a change in the intended population based on the product specifications. Nevertheless, the device indication for use remains the reduction of pregnancy and STD transmission. Therefore, the indications is ostensibly *the same.*

3. A description of the device **MODIFICATION(S),** including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

   This change was for *the addition of a desensitizer lubricant to the previously cleared male latex condom (K952415). The male desensitizer lubricant used is Benzocaine cream (5% w/w) in a polyethylene glycol base. The water soluble lubricant containing benzocaine, an over-the-counter drug recognized as safe and effective under 21 CFR Part 348 for exernal analgesic drug products for OTC human use.*

   The parent company for the SSL-Americas, Inc. (Schmid Laboratories) received marketing clearance for a male latex condom with desensitizing cream under premarket notification (K822088).

   The product has the same characteristics such as the following:
   Similar product features
   Both are made from natural rubber latex
   Designed to conform with the same set of applicable standards for male latex condoms
   Both lubricated with desensitizer-containing benzocaine as active ingredient, though differ in formulation and dosing method for the benzocaine cream and the latex condom formulation.

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including, labeling, intended use, physical characteristics, and *the condom is a straight-walled, nipple-end with a nominal length of 180 mm and a width of 52 mm meeting the requirements of ASTM D-3492-97.* The condoms will be packaged in individual sealed foil packages within an outer consumer carton with a package insert.

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The lubricant system used with this latex condom includes both the silicone lubricant cleared through K952415 in addition to the desensitizing cream which is added to the inner surface of the condom. The condom with have:

Same intended use
Same latex based product
Similar product features
All made with benzocaine contained desensitizer as analgesic.

The device is a latex condom having the same design characteristics as the predicate device:

	DUREX® Latex Condom
Nominal Length	170 mm
Nominal Flat Width	50 mm
Nominal Thickness	0.065 mm
Dusting Powder	Calcium, Magnesium Carbonate
Burst Test Volume	18 Liter min.
Burst Test Pressure	1.0 kPa min.

5. A **Design Control Activities Summary** which includes:
   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis
   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied
   c) A declaration of conformity with design controls. The declaration of conformity should include:
      i) A statement signed by the individual responsible, that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met, and
      ii) A statement signed by the individual responsible, that the manufacturing facility is in conformance with design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.

The application Attachment VI includes Design Risk Analysis that meets the intent of the Risk Analysis methods and is used to assess the impact of the modification on the device.

Included as part of the application is a description of the "Quality Plan" which is a summary of the Quality Control Activities. This document includes and provides for raw material and product specifications, formula and regulatory requirements including safety requirements. This condom is manufactured, processed, packaged and tested in accordance with existing procedures. All of the raw material for the condom and lubricant have not changed; therefore, there are no compatibility or stability issues that needed to be addressed. The only design specification affected by the change is the addition of the benzocaine cream to the condom. The application and specifically this section (design controls) includes an analysis of the potential for excess dosing, microbial contamination, irritation potential (labeling), and stability.

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The application includes a declaration of conformity that the condom with benzocaine , "...on design qualifying basis, meets all our manufacturing requirements that all verification and/or validation activities were performed by the designee and the results demonstrate that the predetermined acceptance criteria were met; and the manufacturing facility is in conformance with the design control procedure requirements."

The statement that manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 is included within this document (Attachment VII).

6. Administrative Elements:

Truthful and Accurate Statement:	Page 8
510(k) Summary or Statement:	Page 17
Indications for Use:	Page 9

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, the device application can be determined substantially equivalent to the previously cleared (or their pre-amendment) device.

J. Michael Kuchinski — 3/28/02 (Date)

Colin M. Pollard, Chief, OGDB — 3/29/02 (Date)

revised:3/27/98

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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SCREENING CHECKLIST
FOR ALL PREMARKET NOTIFICATION [510(k)] SUBMISSIONS

510(k) Number: K020659

The cover letter clearly identifies the type of 510(k) submission as (Check the appropriate box):

- ☒ Special 510(k) - Do Sections 1 and 2
- ☐ Abbreviated 510(k) - Do Sections 1, 3 and 4
- ☐ Traditional 510(k) or no identification provided - Do Sections 1 and 4

Section 1: Required Elements for All Types of 510(k) submissions:

	Present	Inadequate or Missing
Cover letter, containing the elements listed on page 3-2 of the Premarket Notification [510)] Manual.	✓	
Table of Contents.	✓	
Truthful and Accurate Statement.	✓	
Device's Trade Name, Device's Classification Name and Establishment Registration Number.	✓	
Device Classification Regulation Number and Regulatory Status (Class I, Class II, Class III or Unclassified).	✓	
Proposed Labeling including the material listed on page 3-4 of the Premarket Notification [510)] Manual.	✓	
Statement of Indications for Use that is on a separate page in the premarket submission.	✓	
Substantial Equivalence Comparison, including comparisons of the new device with the predicate in areas that are listed on page 3-4 of the Premarket Notification [510)] Manual.	✓	
510(k) Summary or 510(k) Statement.	✓	
Description of the device (or modification of the device) including diagrams, engineering drawings, photographs or service manuals.	✓	
Identification of legally marketed predicate device. *	✓	
Compliance with performance standards. * [See Section 514 of the Act and 21 CFR 807.87 (d).]	NA	
Class III Certification and Summary. **	NA	
Financial Certification or Disclosure Statement for 510(k) notifications with a clinical study. * [See 21 CFR 807.87 (i)]	NA	
510(k) Kit Certification ***	NA	

* - May not be applicable for Special 510(k)s.
** - Required for Class III devices, only.
*** - See pages 3-12 and 3-13 in the Premarket Notification [510)] Manual and the Convenience Kits Interim Regulatory Guidance.

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Section 2: Required Elements for a SPECIAL 510(k) submission:

	Present	Inadequate or Missing
Name and 510(k) number of the sponsor's own, unmodified predicate device.	✓	
A description of the modified device and a comparison to the sponsor's predicate device.	✓	
A statement that the intended use(s) and indications of the modified device, as described in its labeling, are the same as the intended uses and indications for the sponsor's unmodified predicate device.	✓	
A statement that the modification has not altered the fundamental technology of the sponsor's predicate device.	✓	
A Design Control Activities Summary that includes the following elements (a-e):		
a. Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.	✓	
b. Based on the Risk Analysis, an identification of the required verification and validation activities, including the methods or tests used and the acceptance criteria to be applied.	✓	
c. A Declaration of Conformity with design controls that includes the following statements:	✓	
A statement that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results of the activities demonstrated that the predetermined acceptance criteria were met. This statement is signed by the individual responsible for those particular activities.	✓	
A statement that the manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review. This statement is signed by the individual responsible for those particular activities.	✓	

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Section 3: Required Elements for an ABBREVIATED 510(k)* submission:

	Present	Inadequate or Missing
For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type. (If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.)		
For a submission, which relies on a recognized standard, a declaration of conformity [For a listing of the required elements of a declaration of conformity, SEE **Required Elements for a Declaration of Conformity to a Recognized Standard,** which is posted with the 510(k) boilers on the **H drive.**]		
For a submission, which relies on a recognized standard without a declaration of conformity, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has <u>not</u> been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device <u>and</u> any additional information requested by the reviewer in order to determine substantial equivalence.		
Any additional information, which is not covered by the guidance document, special control, recognized standard and/or non-recognized standard, in order to determine substantial equivalence.		

* - When completing the review of an abbreviated 510(k), please fill out an Abbreviated Standards Data Form (located on the H drive) and list all the guidance documents, special controls, recognized standards and/or non-recognized standards, which were noted by the sponsor.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Section 4: Additional Requirements for ABBREVIATED and TRADITIONAL 510(k) submissions (If Applicable):

	Present	Inadequate or Missing
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:		
b) Sterilization and expiration dating information:		
i) sterilization process		
ii) validation method of sterilization process		
iii) SAL		
iv) packaging		
v) specify pyrogen free		
vi) ETO residues		
vii) radiation dose		
c) Software Documentation:		

Items with checks in the "Present but Deficient" column require additional information from the sponsor. Items with checks in the " Missing" column must be submitted before substantive review of the document.

Passed Screening ✓ Yes ____ No
Reviewer: Kuramada
Concurrence by Review Branch: 15

Date: _____

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		✓
2. Did we grant expedited review?	NA	
3. Have you verified that the Document is labeled Class III for GMP purposes?	✓	✓
4. If, not, has POS been notified?	✓	
5. Is the product a device?		✓
6. Is the device exempt from 510(k) by regulation or policy?		
7. Is the device subject to review by CDRH?		✓
8. Are you aware that this device has been the subject of a previous NSE decision?		
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		✓
10. Are you aware of the submitter being the subject of an integrity investigation?		
11. If, yes, consult the ODE Integrity Officer.		
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

March 01, 2002

SSL AMERICAS, INC.
3585 ENGINEERING DR.; STE 200
P.O. BOX 926090
NORCROSS, GA 30092
ATTN: JOYCE NING

510(k) Number: K020659
Received: 01-MAR-2002
Product: DUREX LATEX CONDOM WITH MALE GENITAL DESENSITIZER LUBRICANT

The Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

As a reminder, we would like to mention that FDA requires all 510(k) submitters to provide an indications for use statement on a separate page. If you have not included this indications for use statement in addition to your 510(k) summary (807.92), or a 510(k) statement (807.93), and your Truthful and Accurate statement, please do so as soon as possible. If the above mentioned requirements have been submitted, please do not submit them again. There may be other regulations or requirements affecting your device such as Postmarket Surveillance (Section 522(a)(1) of the Act) and the Device Tracking regulation (21 CFR Part 821). Please contact the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) at the telephone or web site below for more information.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC)(HFZ-401) at the above letterhead address. Correspondence sent to any address other than the DMC will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official. Any telefaxed material must be followed by a hard copy to the DMC (HFZ-401).

You should be familiar with the manual entitled, "Premarket Notification 510(k) Regulatory Requirements for Medical Devices" available from DSMICA. If you have other procedural or policy questions, or want information on how to check on the status of your submission (after 90 days from the receipt date), please contact DSMICA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsmamain.html or me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Staff
Office of Device Evaluation

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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K020659

SSL Americas, Inc.

JOYCE NING
Vice President Regulatory Affairs

3585 Engineering Drive, Suite 200
P.O. Box 926090
Norcross, GA 30092-9214

Dir. Tel: 770-582-2152
Dir. Fax: 770-582-2204
joyce.ning@ssl-americas.com

February 28, 2002

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RECEIVED
MAR 1 11 53 AM '02
FDA/CDRH/ODE/DMC

RE: **Special 510(K) Pre-Market Notification**
DUREX® Latex Condom with Male Genital Desensitizer Lubricant

Gentlemen,

In pursuance to the requirements of 21 CFR, Part 807.87 and in accordance with Section 510(K) of the Federal Food, Drug, and Cosmetic Act, SSL Americas, Inc. is notifying the Food and Drug Administration of its intent to market a DUREX® Latex Condom with Male Genital Desensitizer Lubricant that have been in markets outside of US for many years.

As demonstrated in this submission, this product is substantially equivalent to the numerous other male desensitizer lubricated condoms that are currently in distribution in interstate commerce and does not raise different questions regarding safety and effectiveness. As required by SMDA of 1990, a summary of the safety and effectiveness information upon which the substantial equivalence determination is based is also included the submission.

The content and format of this submission is consistent with those indicated in "Information for a Latex Condom 510(k) Submission for Obstetrics-Gynecology Devices".

SSL considers the existence of this 510(k) Premarket Notification, the data, and other information pertaining to this submission are confidential, and the protection by 18 USC 1905, 21 USC 331 (j), 5 USC 552, and other applicable laws is hereby afforded.

Please feel free to contact me at 770-582-2152 if you have any questions or need any additional information.

Sincerely,

Joyce Ning,
Vice President Regulatory Affairs

JN:jml

OB
II

5K23

SSL Americas, Inc. is a subsidiary of SSL International plc

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

durex® SILIPOS® REGENT

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PART I. TABLE OF CONTENTS – Submission Body

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Attachment II *Packaging Components*

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Attachment VI *Design Risk Analysis*

Attachment VII *Declaration of Conformity*

Attachment VIII *Product stability*

Attachment IX *Biocompatibility*

Reference 1 *Benzocaine Literature Reference – Martindale the Extra Pharmacopoeia 31st Edition.*

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART II. GENERAL INFORMATION

A. NAME AND ADDRESS OF THE APPLICANT

SSL Americas Inc.
3585 Engineering Drive, Suite 200
P. O. Box 926090
Norcross, Georgia 30092-9214

Owner Operator Number: 9004884

B. SIGNATURE OF THE APPLICANT

Name: Joyce Ning
Title: Vice President, Regulatory Affairs

Phone: 770.582.2152
Fax: 770.582.2204

C. ESTABLISHMENT REGISTRATION NUMBER OF SUBMITTER

1065445

D. NAME AND ADDRESS OF MANUFACTURING SITE(S)

London International Group MFY, S.A.
(A Division of London International Group / SSL International)
Avda. Can Fatjo, 151 0891 Rubi
Barcelona, Spain

Site Registration Number: 9617265

E. DEVICE NAME

Proprietary Name: DUREX® Latex Condom with Male Genital Desensitizer Lubricant
Common Name: Latex Condom
Classification Name: Condom (21CFR §884.5300)

F. DEVICE CLASSIFICATION

Class II 21CFR 884.5300

G. REASON FOR 510(K) SUBMISSION

Initial import into USA

H. IDENTIFYING NUMBERS

501(k) Number to be assigned.

I. PREDICATE DEVICE NAME

DUREX® Hispano Ico Latex Condom (K952415)
Desensitized Male Condom (K822088)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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J. PERFORMANCE STANDARDS

ASTM and related standards as referenced in this submission.

H. ENVIRONMENTAL IMPACT

In conformance with the National Environmental Policy Act, this submission claims categorical exclusion, as provided in 21 CFR 25.24 (e) (4).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART III. SUBMISSION APPLICANT INFORMATION

1.0 Pre-Market Notification 510(k) Submission Applicant

Applicant Name:

SSL Americas Inc.
3585 Engineering Drive
P. O. Box 926090
Norcross, Georgia 30092-9214

Telephone: (770) 582-2222
Fax: (770) 582-2233

Registration Number: 1065445

Device Listing Number:

A new listing has been applied for. DUREX® Latex Condoms were previously listed by London International Group (LIG) as the sole initial distributor. Currently due to the merger of the business, LIG Regent Medical has become a division of SSL. (LIG Registration Number is 1039703 and the Device Listing Number is B005146.)

1.1 Activity of Applicant

Initial Distributor, Specification Developer

1.3 Contact Person

Joyce Ning,
Vice President, Regulatory Affairs

Telephone: (770) 582-2152
Fax: (770) 582-2204

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Other Contact Person

Toney Lawrence
Manager Document Control

Telephone: (770) 582-2149
Fax: (770) 582-2233

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART IV: TRUTHFUL AND ACCURATE STATEMENT

2.0

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT
[As required by 21 CFR 807.87(j)]

I certify that, in my capacity as Vice President, Regulatory Affairs of SSL-Americas, I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

Signature

Joyce Ning

Typed Name

Feb 28, 02

Date

Premarket Notification Number

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART V. INDICATIONS FOR USE STATEMENT

3.0

Indications for Use Statement

Applicant: SSL-Americas, Inc.

510(k) Number (if known):* _____

Device Name: DUREX® Latex Condom with Male Genital Desensitizer Lubricant

Indications for Use:

The DUREX® Latex Condom with Male Genital Desensitizer Lubricant is used for contraception and for prophylactic purposes to help reduce the risk of pregnancy and the transmission of sexually transmitted diseases. The male genital desensitizer lubricant on the condom helps in temporarily prolonging the time until ejaculation.

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use _____ **or** **Over-The-Counter Use** _____

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PART VI. SUMMARY OF PRODUCT TECHNICAL INFORMATION

4.0 Device Proprietary or Trade Name

DUREX® Latex Condom with Male Genital Desensitizer Lubricant

4.1 Modification:

This particular application is to add desensitizer lubricant to the previously approved male latex condom cleared under K952415.

The male desensitizer lubricant used is Benzocaine cream of which the composition, manufacturing method, and control testing are detailed in the Section of Attachment I.

The Benzocaine cream is dosed in the teat inside of the condom and being semi-solid remains inside the condom. When this condom is placed over the erect penis, the anaesthetic is then in contact with the glans which is the most sensitive part of the penis and thus prolong duration till ejaculation.

5.0 Name and Location of Actual Manufacturer

London International Group MFY, S.A.
(A Division of London International Group / SSL International)
Avda. Can Fatjo, 151 0891 Rubi
Barcelona, Spain

Registration Number: 9617265

6.0 Device Description

DUREX® Latex Condom with Male Genital Desensitizer Lubricant is made of a natural rubber latex sheath with water soluble lubricant containing Benzocaine, an over-the-counter drug recognized as safe and effective by US FDA under 21 CFR 5300 for condom and 21 CFR Part 348 for external analgesic drug products for over-the-counter human use. The condom is a straight-walled, nipple-end condom with the nominal length of 180 mm and width of 52 mm as required by ASTM D-3492-97.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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6.1 Device Characteristics - Specifications

Condom specifications are summarized as follows.

Nominal Length	170	mm min.
Nominal Width	50	mm min.
Nominal Thickness	0.065	mm min.
Airburst test pressure	1.0	kPa min.
Airburst test Volume	18	Liter min.

This condom meets all of the specification requirements for natural rubber latex condom as indicated in A.S.T.M. Standard D1076-97.

6.2 Materials of the primary package (individual condom packet)

This proposed condom will be supplied in individually sealed foils packaged within an outer consumer carton with a package insert. Refer to Attachment II for packaging component details.

6.3 Lubricant system

In addition to the regular silicone lubricant used on condom as lubricating agent to ease the application, the desensitization lubricant is added to the condom teat for retardation purpose.

The water-soluble lubricant system used for desensitization application on this proposed condom is made of glycerin mixture with benzocaine as active ingredient. The composition and manufacturing details for this lubricant can be found under Attachment I.

7.0 Proprietary and Confidential Product Composition

The latex material composition and additives, other than desensitizer lubricant, are the similar materials used in the previously approved latex condom cleared under K952415.

Refer to Attachment III for the details of these composition and additives.

8.0 Quality Assurance Testing

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Statistical sampling, utilizing Mil Std 105E, performed on each finished condom batch to conduct testing against required standards is detailed in the Standard Operating Procedure referenced under Attachment IV.

All manufacturing and quality control processes/ procedures (Attachment IV), are similar to those of the previously approved predicate (K952415) to ensure product integrity meeting requirements.

9.0 Declaration of Conformity

The proposed condom had been manufactured and commercially distributed for years (refer to the commercial history under Attachment V) with credible safe history. The manufacture of Durex condoms is performed under a quality system certified to meet the requirements of ISO 9001 and EN46001 standards. As part of the design control activities, risk analysis was performed and the report to properly assess the impact of the modification on the device and its component is available under Attachment VI. A copy of the Declaration of Conformity is available under Attachment VII.

10.0 Expiration Date or Quality at Delivery

10.1 Expiration Date

Five-year expiry period is based on the satisfactory testing results, both on finished device and on the benzocaine cream, at controlled storage conditions as required by the stability program. Refer to the stability report under Attachment VIII for details.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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10.2 Quality at Delivery

As indicated in Section 8.0, gloves are subjected to statistical sampling based upon Mil Std 105E for compliance to the requirements to all related A.S.T.M. Standards and other applicable standards referenced in this submission. Together with the above referenced stability results at Section 10.0, the proposed condom's quality at delivery actually exceeds applicable ASTM standards.

11.0 Other Claims

No other claims at the time of this submission.

12.0 Summary Reports of Stability Testing Results

See the above Section, 10.1, for stability testing results exhibited under Attachment VIII.

12.1 Condom safety history

The proposed condom had been manufactured and commercially distributed for years (refer to the commercial history under Attachment V) with credible safe history.

12.2 Safety Reports on Desensitizer Lubricant

The ingredients used in the Benzocaine cream (See Attachment I) are well established and have been used in topical skin products and in condom lubricants for many years, without evidence of significant toxicological reactions. Benzocaine is poorly soluble in water and poorly absorbed, hence the incidence of systemic reactions is low (Reference 1) and no systemic anesthesia will occur. Neither Benzocaine nor ingredients in the cream have known carcinogenic potential properties.

12.3 Biocompatibility

Since the proposed product used the same materials as those used in the predicate previously cleared under 510(k) K 952415, the biocompatibility results of the proposed condom are expected to be

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as satisfactory. To confirm this conclusion, samples of the proposed finished products were submitted for testing for sensitization, primary mucosal irritation, and acute systemic toxicity. The tested results, available under Attachment IX, completed at the time of this submission are evident as safe as expected.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART VII. STATEMENT OF SUBSTANTIAL EQUIVALENCE

Substantial Equivalence Comparison to Predicate Device:

1.0 Primary Predicate Device: SSL own DUREX® Hispano Ico Latex Condom (K952415) and Male Condom with Desensitizer (K822088)

DUREX® Hispano Ico Latex Condom (K952415)

- Durex® male latex condom with desensitizer lubricant is substantially equivalent to own Hispano Ico latex condom in that they provide the same characteristics listed as follows.

  - Same intended use.
  - Same sizes, product features
  - Same packaging
  - Both made of synthetic Rubber Latex
  - Both manufactured using similar manufacturing process.
  - Both designed to conform with same sets of applicable standards for male latex condoms.

- Durex® male latex condom with desensitizer lubricant has been shown to be non-irritable and compatible with the same recommended test requirements for Durex® Hispano Ico latex condom.

- Based on QA testing with Durex® male latex condom with desensitizer lubricant, SSL has found no significant difference with these condoms and the predicate device, Durex® Hispano Ico latex condom. All conform to applicable standards detailed in this submission.

- The only difference is that the proposed condom is dosed with desensitizer lubricant which was not included in this predicate.

Durex® Desensitized Male Latex Condom (K822088)

- Durex® latex condom with male desensitizer lubricant is substantially equivalent to own desensitized male latex condom previously cleared under 510(k), K822088, in that they provide the same characteristics listed as follows.

  - Same intended use

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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- Similar product features
- Both made of synthetic Rubber Latex
- Both designed to conform with same sets of applicable standards for male latex condoms.
- Both lubricated with desensitizer-contained benzocaine as active ingredient, though differ in formulation and dosing method.

- Durex® male latex condom with desensitizer lubricant has been shown to be non-irritable and compatible with the same recommended test requirements for this predicate, the desensitized male latex condom.

- Based on QA testing with Durex® male latex condom with desensitizer lubricant, SSL has found no significant difference with these condoms and the predicate device, Durex® Hispano Ico latex condom. All conform to applicable standards detailed in this submission.

- The only difference is that the proposed condom is made with a variation of the latex formulation and dosed with desensitizer lubricant at the teat (see Attachment I) instead on the wall.

2.0 Secondary Predicate Devices: TROJAN® Latex Condom with Male Desensitizer Lubricant (K000748)

- DUREX® Latex Condom with Male Desensitizer Lubricant is substantially equivalent to the above stated predicate in that they provide the same characteristics listed as follows.

  - Same intended use.
  - Same latex based product
  - Similar product features
  - All made with Benzocaine contained desensitizer as analgesics.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART VIII. 510(K) SUMMARY

Submitter by: SSL Americas, Inc.
3585 Engineering Drive
Norcross, Georgia 30092

Contact Person: Joyce Ning
Vice President, Regulatory Affairs
Phone: (770) 582-2152

Date Prepared: February 15, 2002

Proprietary Name: Durex® latex condom with male desensitizer lubricant

Common Name: Latex Condom

Classification Name: Condom (21 CFR § 884.5300)

Predicate Device: DUREX® Hispano Ico Latex Condom (K952415) and Male Condom with Desensitizer (K822088)

Description of the Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant is made of a natural rubber latex sheath with lubricant containing Benzocaine, an over-the-counter drug recognized as safe and effective by US FDA under 21 CFR 5300 for condom and 21 CFR Part 348 for external analgesic drug products for over-the-counter human use. The condom is a straight-walled, nipple-end condom with the nominal length of 180 mm and width of 52 mm as required by ASTM D-3492-97.

Intended Use of the Device: DUREX® Latex Condom with Male Genital Desensitizer Lubricant has the same intended use as the predicate condom. It is used for contraception and for prophylactic purposes to help reduce the risk of pregnancy and the transmission of sexually transmitted diseases (STDs). In addition, the male genital desensitizer lubricant on the condom helps in temporarily prolonging the time till ejaculation.

Technological Characteristics: Both the proposed device and the predicate device are of the similar design meeting ASTM Standard (D3492) specification for Rubber Contraceptives (Male Condoms). Both are straight-walled, nipple-end, lubricated made with the similar formulation of natural rubber latex. The proposed condom is a modification of the predicate device with variation merely in the lubricant application.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PART IX. PRODUCT PACKAGING AND LABELING

The proposed package labeling pieces are attached as organized:

1. Primary Package Labeling – Individual Package
2. Outer Box Package Labeling – Consumer Box
3. Inner Pouch Labeling – Package Insert

There is no other (promotional) labeling available at the time of this submission.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Primary Package Labeling
Individual Package

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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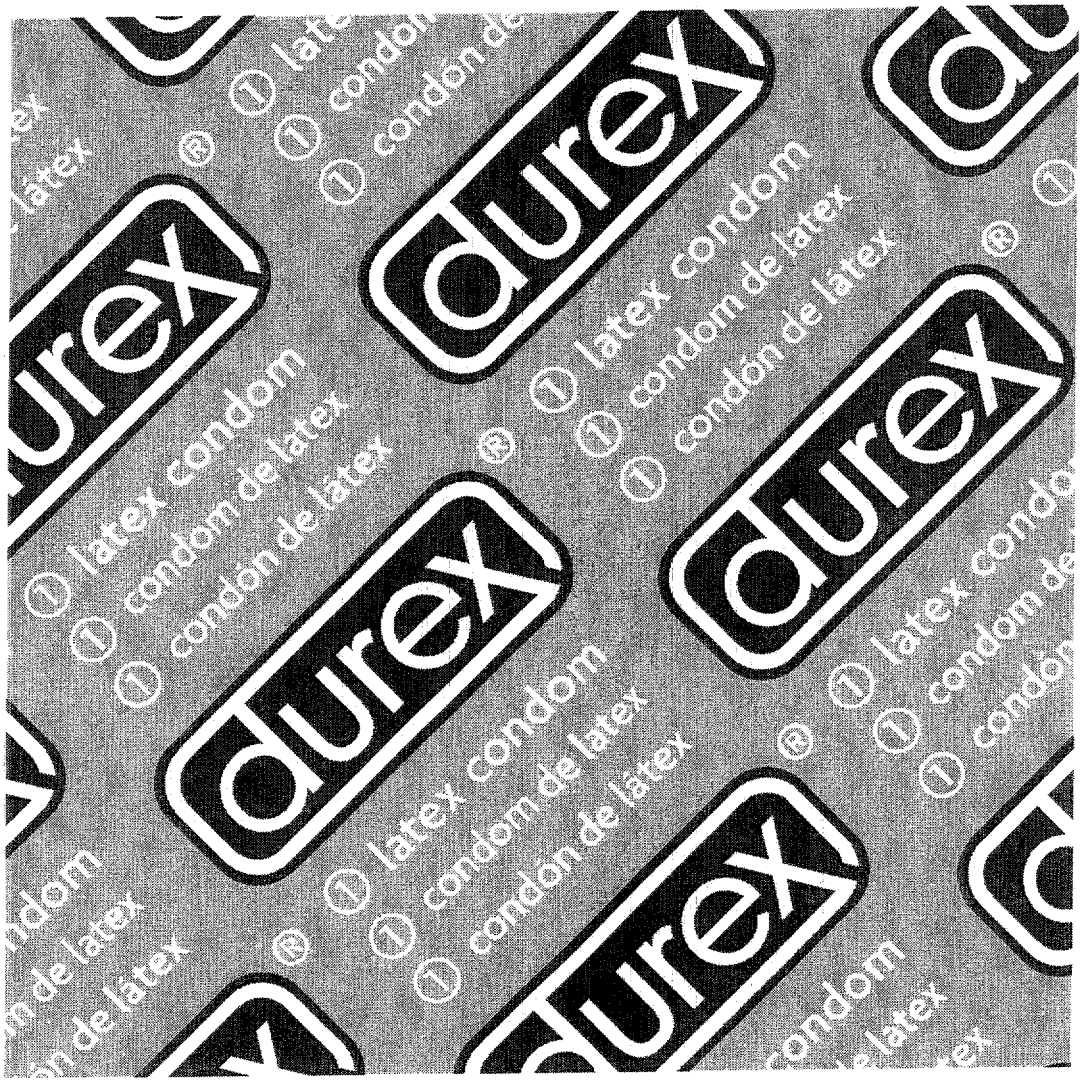

Background Pantone 877c
SILVER

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Distributed by Durex Consumer Products Inc.,
Norcross, GA 30092
011877R Made in Spain

lubricated

CAUTION: This product contains natural rubber latex which may cause allergic reactions.

Effective against pregnancy, HIV (AIDS) and STDS

LOT D00078E Q
Q/EXP 2005-01
MADE IN SPAIN

Distributed by Durex Consumer Products Inc.,
Norcross, GA 30092
011877R Made in Spain

lubricated

CAUTION: This product contains natural rubber latex which may cause allergic reactions.

Effective against pregnancy, HIV (AIDS) and STDS

Distributed by Durex Consumer Products Inc.,
Norcross, GA 30092
011877R Made in Spain

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

Outer Box Package Labeling
Consumer Box

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

Effective Against Pregnancy, HIV (AIDS) & STDs

Prolonged Performance

climax control lubricant for longer lasting pleasure

climax control lubricant

12

Avoid excess heat. Store at room temperature

INSTRUCTIONS INSIDE

NEW!
HELPS TO PROLONG PLEASURE

durex

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Inner Pouch Labeling
Package Insert

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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USA CAN TRIED AND TRUSTED BY MILLIONS OF PEOPLE WORLD-WIDE, DUREX IS THE WORLD'S LEADING CONDOM BRAND.

Do not use oil-based lubricants, such as petroleum jelly or oil-based products. If an additional lubricant is required, ensure that the lubricant is compatible with latex condoms.

Non-vaginal use of condoms may increase the risk of them slipping or being damaged.

If used properly, latex condoms will help to reduce the risk of transmission of HIV infection (AIDS) and many other sexually transmitted diseases, including chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B and syphilis.

If after intercourse you are concerned for whatever reason you or your partner may have become pregnant, contact your doctor immediately.

This product contains natural rubber latex which may cause allergic reactions.

Some individuals may experience sensitivity to latex products. If you are allergic to latex products, please consult your doctor before use.

Some topical medicines may affect the efficacy of latex condoms on contact. Please consult your pharmacist/doctor on the compatibility of these products with condoms prior to use.

Some individuals may experience a slight irritation to spermicides. If this should happen to you please consult a doctor. The *Durex* range also includes non-spermicidal condoms.

No method of contraception can provide 100% protection against pregnancy or the transmission of HIV and sexually transmitted infections.

For more information about *Durex* condoms or the range of *Durex* condoms available in your country, visit our website at www.durex.com or write to;

Durex Canada
Concord, Ontario
L4K 3T6

LIG Head Office
Turnford Place,
Broxbourne EN10 6LN, UK

Durex Consumer Products Inc
Norcross, GA 30092
USA

Durex and the *Durex Seal of Quality* are trademarks of the LI group.

F DUREX, LA MARQUE LEADER DE PRESERVATIFS (CONDOMS) PLEBISCITEE DANS LE MONDE ENTIER PAR DES MILLIONS D'HOMMES ET DE FEMMES.

Ne jamais utiliser de lubrifiants à base d'huile tels que vaseline, beurre, huiles et crèmes de soins. Si la lubrification est insuffisante, utiliser un lubrifiant à base d'eau compatible avec le latex des préservatifs (condoms).

Si ce préservatif (condom) est utilisé autrement que pour un rapport vaginal, il faut savoir qu'il a plus de risques d'être abimé ou de glisser.

Un préservatif (condom) correctement utilisé aide à réduire le risque de transmission du virus VIH (SIDA) et des autres maladies sexuellement transmissibles, telles que les chlamydia, herpès et verrues génitales, gonorrhée, hépatite B ou syphilis.

S'il y a un risque que vous ou votre partenaire soyez enceinte par suite d'un oubli ou d'une erreur d'utilisation d'un moyen de contraception, consultez un médecin immédiatement.

Ce produit contient du caoutchouc naturel de latex qui peut causer des réactions allergiques. Certaines personnes peuvent être sensibles aux produits en latex. Dans ce cas, consulter son médecin avant emploi.

Certains produits (médicaments ou autres) peuvent altérer l'efficacité du préservatif (condom). Avant utilisation, toujours vérifier leur compatibilité auprès de votre pharmacien ou médecin.

Certaines personnes peuvent ressentir une légère irritation due aux spermicides. Si c'était le cas pour vous ou votre partenaire, ne pas hésiter à consulter un médecin. La gamme *Durex* propose aussi des préservatifs (condoms) sans spermicide.

Aucune méthode de contraception ne peut garantir une protection à 100 % contre la grossesse, contre le virus VIH (SIDA) ou les autres maladies sexuellement transmissibles.

Pour plus d'informations sur les préservatifs (condoms) *Durex* disponibles dans votre pays et leurs spécificités, consultez notre site internet: www.durex.com ou écrivez-nous à:

LIG France S.A.
11, avenue Dubonnet
92407 Courbevoie Cedex
France

Durex et le *sceau de qualité Durex* sont des marques du groupe LI.

E MILLONES DE PERSONAS EN TODO EL MUNDO YA HAN PROBADO Y CONFIAN EN LOS PRESERVATIVOS DUREX

No usar lubricantes en base de aceite, como vaselina ni óvulos vaginales en base de aceite. Si necesita un lubricante adicional, asegúrese de que el lubricante sea compatible con preservativos de látex.

El uso no vaginal de los preservativos puede incrementar el riesgo de deterioro o desprendimiento del mismo.

Cuando se usan adecuadamente, los preservativos de látex ayudan a reducir el riesgo de transmisión de la infección del VIH (SIDA) así como muchas enfermedades de transmisión sexual como clamidia, herpes genitales, verrugas genitales, gonorrea, hepatitis B y sífilis.

Este producto contiene látex de caucho natural, el cual puede causar reacciones alérgicas.

Si después de la relación sexual considera, por cualquier razón, que usted o su pareja puede haberse quedado embarazada, consulte a su médico inmediatamente.

Algunas personas pueden experimentar sensibilidad a los productos de látex, por favor consulte a su médico antes de usar el preservativo.

Algunos medicamentos de aplicación tópica pueden afectar la eficacia de los preservativos de látex. Consulte a su farmacéutico/médico acerca de la compatibilidad de estos productos con los preservativos antes del uso.

Algunas personas pueden experimentar una ligera irritación a espermicidas. Si esto le ocurriese a usted o su pareja, consulte a su médico. La gama de preservativos *Durex* también incluye preservativos sin espermicida.

Ningún método de anticoncepción puede proporcionar el 100% de protección frente al embarazo, SIDA o enfermedades de transmisión sexual. Para más información acerca de los preservativos *Durex* o la gama de preservativos *Durex* disponibles en su país, visite nuestra dirección de web en www.durex.com u escriba a:

Para Latinoamérica
DUREX Consumer
3585 Engineering Drive,
Norcross, Georgia 30092 USA

Durex y el *sello de calidad Durex* son marcas del grupo LI.

P MILHÕES DE PESSOAS EM TODO OMUNDO JÁ EXPERIMENTARAM E CONFIAM NOS PRESERVATIVOS DUREX

Não usar lubrificantes de base oleosa, como a vaselina, nem óvulos vaginais de base oleosa. Caso necessite de um lubrificante adicional, assegure-se da sua compatibilidade com os preservativos em látex.

O uso não vaginal dos preservativos pode aumentar o risco de deterioração ou desprendimento do mesmo.

Quando usados adequadamente, os preservativos ajudam a reduzir o risco de transmissão da infecção por HIV (SIDA), assim como muitas doenças de transmissão sexual como clamídias, herpes genital, verrugas genitais, gonorreia, hepatite B e sífilis.

Este produto contem látex natural que pode ocasionar reacções alérgicas.

Se depois da relação sexual, algum dos elementos do casal, por qualquer razão, tiver receio de que a parceira possa ter ficado grávida, esta deverá dirigir-se ao seu médico imediatamente.

Algumas pessoas podem experimentar sensibilidade aos produtos em látex. Por favor consulte o seu médico antes de usar o preservativo.

Alguns medicamentos de aplicação tópica podem afectar a eficácia dos preservativos de látex. Consulte o seu farmacêutico/médico acerca da compatibilidade destes produtos com os preservativos.

Algumas pessoas podem experimentar uma ligeira irritação a espermicidas. Se isto ocorrer consigo ou com a sua parceira, consulte o médico. A gama de preservativos *Durex* também inclui preservativos sem espermicida.

Nenhum método de contracepção pode proporcionar 100% de protecção contra a gravidez, SIDA ou doenças sexualmente transmissíveis.

Para mais informação acerca dos preservativos *Durex* ou da gama de preservativos *Durex* disponíveis no seu país, visite a nossa direcção de web em www.durex.com ou escreva para;

LRC Laboratórios, Lda.
Rua Rodrigues Sampaio, 97-3º
1169-121 Lisboa

Durex e o *Selo de Qualidade Durex* são marcas do Grupo LI.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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USA CAN **Please read this instruction leaflet carefully**

HOW TO USE A CONDOM

Handle with care. Condoms can be torn by fingernails and sharp objects such as jewellery, zips and buckles.

F **Lire attentivement le mode d'emploi.**

COMMENT UTILISER UN PRÉSERVATIF (CONDOM)

Manipuler le préservatif (condom) avec précaution. Faire attention aux ongles et aux objets coupants (bagues, fermetures éclairs, boucles de ceinture), qui pourraient endommager le préservatif (condom).

E **Por favor lea detenidamente este folleto de instrucciones.**

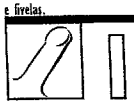
INSTRUCCIONES DE USO

Manipular con cuidado. El preservativo puede dañarse con las uñas y objetos cortantes como anillos, cremalleras, hebillas etc...

P **Por favor leia atentamente este folheto de instruções.**

INSTRUÇÕES DE USO

Manipule com cuidado. O preservativo pode danificar-se com as unhas e objectos cortantes como anéis, fechos de correr e fivelas.



1

USA CAN Put the condom on when the penis is erect, before there is any contact between the penis and your partner's body. Fluid released from the penis during the early stages of an erection can contain sperm and organisms that can cause STDs.

F Mettre le préservatif (condom) en place quand le pénis est entièrement en érection et avant tout contact entre le pénis et le corps du partenaire. Le liquide émis pendant les préliminaires sexuels peut contenir des spermatozoïdes et des germes contaminants.

E Coloque el preservativo sobre el pene erecto, antes de que haya cualquier tipo de contacto entre el pene y el cuerpo de su pareja. Los fluidos producidos durante las primeras fases de la erección pueden contener esperma y microorganismos causantes de ETS.

P Coloque o preservativo sobre o pénis erecto e antes de qualquer contacto com a sua parceira. Os fluidos pré-ejaculatórios nas primeiras etapas de uma erecção podem conter esperma ou microorganismos causadores de DST.

2

USA CAN Tear along one side of the foil being sure not to rip the condom inside. Carefully remove the condom.

F Ouvrir délicatement l'emballage en le déchirant sur un côté. S'assurer que le préservatif (condom) à l'intérieur ne soit pas endommagé.

E Abra el envase por un lado, teniendo especial cuidado de no dañar el preservativo. Sáquelo cuidadosamente del envase.

P Abra o invólucro por um dos lados, tendo especial cuidado para não danificar o preservativo. Retire-o cuidadosamente do invólucro.

3

USA CAN Air trapped inside a condom could cause it to break. To avoid this, squeeze the closed end of the condom between your forefinger and thumb and place the condom over the erect penis. Be sure that the roll is on the outside.

F L'air resté à l'intérieur du préservatif (condom) peut provoquer sa rupture. Veillez donc à saisir soigneusement entre les doigts le haut du préservatif (condom)-le réservoir-afin de chasser l'air. Placer le préservatif (condom) sur le bout du sexe en érection. S'assurer que la partie à dérouler est à l'extérieur.

E El aire atrapado dentro del preservativo puede causar su rotura. Para evitarlo, apriete el extremo cerrado del preservativo entre los dedos índice y pulgar y coloque el condón sobre el pene erecto. Asegúrese de que la parte enrollada se encuentre en el lado exterior.

P O ar retido dentro do preservativo pode causar a sua rotura. Para o evitar, aperte o preservativo pelo depósito, entre o dedo polegar e o indicador e coloque o preservativo sobre o pénis erecto. Assegure-se de que o rolo fica do lado exterior.

4

USA CAN While still squeezing the closed end, use your other hand to unroll the condom gently down the full length of the penis.

Make sure the condom stays in place during sex; if it rolls up, roll it back into place immediately. If the condom comes off, withdraw the penis and put on a new condom before intercourse continues.

F En maintenant toujours le réservoir entre les doigts, utiliser l'autre main pour continuer à dérouler complètement le préservatif (condom) le long du pénis.

S'assurer que le préservatif (condom) reste en place pendant la relation sexuelle. S'il s'enroule sur lui-même pendant l'acte, le replacer immédiatement en le déroulant à nouveau. Si le préservatif (condom) s'enlève entièrement, en mettre un nouveau avant de continuer la relation sexuelle.

E Mientras sigue presionando el extremo cerrado del preservativo con una mano, use la otra mano para desenrollarlo cuidadosamente hasta cubrir totalmente el pene.

Asegúrese que el preservativo se mantiene en su sitio durante la relación sexual; en el caso de que se enrolle durante la relación, desenróllelo de nuevo inmediatamente. En caso de que el preservativo se desprenda, retire el pene y coloque un preservativo nuevo antes de continuar la relación sexual.

P Enquanto continua a pressionar o preservativo com uma mão, use a outra para o desenrolar cuidadosamente até cobrir totalmente o pénis.

Assegure-se de que o preservativo se mantém no sítio durante a relação sexual; se este se enrolar durante a relação, coloque-o de novo no seu sítio imediatamente. Caso o preservativo se desprenda, retire o pénis e coloque um preservativo novo antes de continuar a relação sexual.

5

USA CAN Soon after ejaculation, withdraw the penis while it is still erect by holding the condom firmly in place. Remove the condom only when the penis is fully withdrawn.

Keep both the penis and condom clear from contact with your partner's body.

F Se retirer après l'éjaculation et avant la fin de l'érection, tout en retenant le préservatif (condom) à la base du sexe. Attendre de s'être complètement retiré avant d'enlever le préservatif (condom). Veiller encore à éviter tout contact du pénis et du préservatif (condom) usagé avec le corps du partenaire.

E Tras la eyaculación, retire el pene mientras todavía esté erecto, sujetando firmemente el preservativo en su sitio. Retire únicamente el preservativo después de haber sacado completamente el pene. Mantenga tanto el pene como el preservativo alejado del cuerpo de su compañera.

P Após a ejaculação, retire o pénis antes de ter desaparecido a erecção, apertando o preservativo pela base de modo a assegurar que não sai sémen ao ser retirado.

Evite que o sémen entre em contacto com a sua parceira mantendo o pénis e o preservativo afastado da mesma.

6

USA CAN Dispose of the used condom hygienically. Wrap the condom in a tissue and place it in the trash (do not flush it down the toilet).

NEVER USE A CONDOM MORE THAN ONCE

F Jeter le préservatif (condom) de façon hygiénique: le rouler dans un papier et le mettre à la poubelle. Ne pas le jeter dans les toilettes.

UN PRESERVATIF (CONDOM) NE S'UTILISE QU'UNE SEULE FOIS

E Deseche el preservativo higiénicamente. Enrolle el preservativo usado en un papel y tírelo en la basura (nunca en el inodoro)

NUNCA USE UN PRESERVATIVO MAS DE UNA VEZ

P Liberte-se do preservativo de forma higiénica. Enrole o preservativo usado num papel e deite-o no lixo (nunca no W.C)

NUNCA USE UM PRESERVATIVO MAIS DO QUE UMA VEZ

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Attachment I
Desensitizer Lubricant Related Information

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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FILE REFERENCE TF/QA/023	ISSUE: 0	SECTION: 2 QUALITATIVE & QUANTITATIVE PARTICULARS	PAGE 1 of 1
TITLE: SUPPORT DATA SUPPLIED TO THE AUSTRALIAN TGA FOR THE USE OF BENZOCAINE AS A MALE DESENSITIZING AGENT ON CONDOMS			
ACCOUNTABLE MANAGER: J. José European Regulatory Affairs Manager		DATE: 21-9-01	COPY No:
This is a controlled document. Do not copy or amend. Contact the Regulatory Affairs Department at Cambridge for assistance or further copies.			

2. QUALITATIVE & QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

The active ingredient in the retarding cream used in Durex Performa condoms is benzocaine which is purchased to USP and BP pharmacopoeial requirements (see attached). The formulation of the cream is as follows:

Benzocaine cream

w/w

(b)(4) [redacted]

No materials of animal origin are used in the above formulation.

During lubrication/packing of the c[redacted] ([redacted] enzocaine cream is added to the inside of the condom teat. There will therefore be a (b)(4) [redacted] 0mg benzocaine in each condom.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b)(4)

[redacted]

USP 1995.

(b)(4)

(b)(4)

[redacted]

Records processed under FOIA Request #2015-4705, Released by CDRH on 3/7/2016

3. METHOD OF MANUFACTURE

3.1 Benzocaine cream

(b)(4) [redacted]

The cream is fully tested to an agreed specification prior to approval for use.

3.2 Addition of the Benzocaine cream to the condom

This is an automated process. (b)(4) [redacted]

(b)(4) [redacted]

All SSL International condom manufacturing sites operate under quality systems certified to the ISO 9000/EN46000 series of standards by the Notified Body BSI in the UK.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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4. CONTROL TESTS ON THE FINISHED PRODUCT

The Benzocaine cream is produced to meet the following specification. Each batch must meet these requirements before release.

Physical tests

Appearance:

Colour:

Odour:

Specific Gravity (25°C):

Viscosity (25°C):

pH (5% aqueous solution):

Microbiology tests

Total Viable Count:

Pathogenic micro-organisms:

Chemical test

Benzocaine content:

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Attachment II
Packaging Components

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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RAW MATERIAL SPECIFICATION				
Doc. Ref. GQA/RM/002A	Issue: 0	Date: Draft 1	Copy No:	Page 1 of 2

SUBJECT: CONDOM FOIL

1. SUPPLIER

(b)(4) [redacted]

2. SPECIFICATION

a) (b)(4) [redacted]

b) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b)(4)

[redacted]

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d)

e)

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3. STORAGE CONDITIONS

Store in a cool dry place out of direct sunlight.

4. SHELF LIFE

5 years

5. GOODS INWARDS TEST

A Certificate of Analysis should be provided with each delivery according to the signed specifications.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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REVISION NUMBER	TITLE: REVISION RECORD SHEET	DOC. REF: GQA/RM/002	
	DESCRIPTION	DOCUMENT CHANGE CONTROL REF. NUMBER	DATE
0	New specification	C.01.023	

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(b)(4)

[redacted]

DOCUMENT CODE: SP/PM/S/12/1

Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

ATTACHMENT III

TABLE 1 – Latex Formulation Summary

Chemical Composition	CAS Number	Percentage Range: PHR	Function
Natural Dry Latex	(b)(4) [redacted]		
Dry Latex-High Ammonia			
Colloidal Sulfur			
Robac Z.D.B.C.			
Zinc Oxide			
Irganox 1330			
Casin			
Darvan			
Potassium Oleate			
Emu;gin B2			
Potassium Hydroxide			
Sodium Bentonite			
Ammonium Hydroxide 25%			
Dowicil 200			

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ATTACHMENT III

TABLE 2 – Color Summary

Color	CI No.	CAS Number	21CFR Citation	Amount
Clear	-	-	-	-

TABLE 3 – Other Additives

Chemical Composition	Supplier	CAS Number	Amount
Lubricant - Silicone	(b)(4) [redacted]		
Desensitizer - Benzocaine			
Dusting Agent –Calcium, Magnesium Carbonate			

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Attachment IV
Quality Plan

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

(b)(4)

[redacted]

Qu

QUALITY PLAN - USA PRODUCT

[redacted]

Records processed under (b)(4)

Questions? Contact FDA/CDR

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QUALITY PLAN - INWARDS

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

QUALITY PLAN - INWARDS

[redacted]

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Questions? Co

QUALITY PLAN - COMPOUNDING

[redacted]

(b)(4)

Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

SSL Healthcare Manufacturing, S.A.

QUALITY PLAN - DIPPING

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

69

[redacted]

(b)(4)

[redacted]

(b)(4)

[redacted]

(b)(4)

72

[redacted]

(b)(4)

[redacted]

(b)(4)

SSL Healthcare Manufacturing, S.A.

QUALITY PLAN - FOILING

DOCUMENT CODE:	QS/MP/QSE/i/5/25
PAGE: 1	OF: 4

		RESPONSIBILITY	METHOD	RECORD
[redacted]				

(b)(4)

[redacted]

(b)(4)

[redacted]

(b)(4)

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(b)(4)

[redacted]

SSL Healthcare Manufacturing, S.A.

QUALITY PLAN - FOILING

DOCUMENT CODE: QS/MP/QSE/I/5/25

PAGE: 4 OF: 4

Questions? Contact FDA/CDRH

QUALITY PLAN - FINISHED PRODUCT

[redacted]

(b)(4)

[redacted]

(b)(4)

[redacted]

(b)(4)

QUALITY PLAN - ELECTRONIC TESTING

[redacted]

(b)(4)

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Attachment V
Commercial History

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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ATTACHMENT V

Commercial History

Benzocaine-lubricated condoms have been marketed by SSL (formerly London International Group, LIG) in Europe (Spain, Italy, Greece), Turkey and the USA for a number of years, and launched more recently in the UAE.

In Europe, this lubricated condom is marketed under the name of " Retardante" condom which is a CE marked medical device with sales of over 26,300,000 condoms in the period 1988 through September of 2001. During this period of time, there were only four reports of adverse events have been received, none of them related to Benzocaine. These adverse events are listed as follows.

Breakage	2
Dryness	1
Objection to color	1

This brand name, Retardante, is now re-branded to "Durex Performa".

SSL also hold a 510(k) approval for a Benzocaine lubricated condom which has slight variation in condom formulation than the proposed condom. Nevertheless, the active ingredient for Benzocaine is the same. This is the second predicate (K 822088) approved in 1982, the Desensitized Male Condom, indicated in this application. This product was in market for years also with a low incident rate of complaints. There have been no recalls relating to the device in any of the above markets.

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Attachment VI
Design Risk Analysis

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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9. RISK ANALYSIS

(b)(4)

[redacted]

FOR INFORMATION ONLY

Table 1: Hazard Quantification

Example	Rating
Death	(b)(4) [redacted]
Serious injury	
Injury	
Minor injury	
Delay	
Inconvenience	

Table 2: Likelihood Quantification

Example	Rating
Very likely during a procedure	(b)(4) [redacted]
Likely during a procedure	
Not likely during a procedure	
Not likely during 10 procedures	
Not likely during product life	

Using these ratings the potential risk for each hazard can be calculated as follows:

Risk = Hazard x Likelihood of occurrence.

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Hazard	Hazard Rating	Likelihood	Risk	Comment
(b)(4) [redacted]				

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Attachment VII
Declaration of Conformity

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Declaration of Conformity

I certify that the finished proposed DUREX® Latex Condom with Male Genital Desensitizer Lubricant; on design qualifying basis, meets all our manufacturing requirements that all verification and/or validation activities were performed by the designee(s) and the results demonstrated that the predetermined acceptance criteria were met; and the manufacturing facility is in conformance with the design control procedure requirements.

Signature

FERNANDO PUEYO

Typed Name

13 - 2 - 2002

Date

Premarket Notification Number

510(k) Premarket Notification
Submitted February 7, 2002

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Attachment VIII
Product Stability

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5. STABILITY

5.1 Compatibility of benzocaine cream with the condoms

(b)(4)

[redacted]

5.2 Benzocaine stability – accelerated data

(b)(4)

[redacted]

5.3 Benzocaine stability – real time/accelerated data

(b)(4)

[redacted]

Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Attachment IX
Biocompatibility

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

(b)(4)

[redacted]

STUDY TITLE:

ISO ACUTE SYSTEMIC TOXICITY STUDY IN THE MOUSE

(Extract)

TEST ARTICLE:

Benzocaine Latex Condom

IDENTIFICATION NO.:

B0136AC

(b)(4)

[redacted]

(b)(4)

[redacted]

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(b)(4)

[redacted]

(b)(4)

[redacted]

SUMMARY

(b)(4)

[redacted]

(b)(4)

[redacted]

(b)(4)

[redacted]

INTRODUCTION

The test article identified below was extracted and the extract was evaluated for biocompatibility in accordance with the requirements of the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 11: Tests for Systemic Toxicity. The purpose of the study was to determine whether leachables extracted from the material would cause acute systemic toxicity following injection into mice. The test article was received on January 11, 2002. The animals were dosed on January 22, 2002, and the observations were concluded on January 25, 2002.

MATERIALS

(b)(4) Test Data

[redacted]

(b)(4)

[redacted]

Justification of Test System:

(b)(4) Test Data

[redacted]

(b)(4)

[redacted]

Evaluations and Statistics:

(b)(4) Test Data

[redacted]

(b)(4)

(b)(4) Test Data

(b)(4) Test Data

(b)(4)

[redacted]

STUDY TITLE:

ISO VAGINAL IRRITATION STUDY IN THE RABBIT

(Repeated Exposure, Extract)

TEST ARTICLE:

Benzocaine Latex Condom

IDENTIFICATION NO.:

B0136AC

(b)(4) Test Data

[redacted]

(b)(4)

[redacted]

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(b)(4) Test Data

[redacted]

(b)(4)

[redacted]

SUMMARY

(b)(4) Test Data

[redacted]

(b)(4) Test Data

[redacted]

(b)(4)

[redacted]

INTRODUCTION

A vaginal irritation study of the test article identified below was conducted in the rabbit. The purpose of the study was to evaluate the potential for mucosal tissue irritation of material extracts administered intravaginally to rabbits for 5 days (see DEVIATION). The test article was received on January 11, 2002. Animal treatment began on January 25, 2002, and the vaginal tissue was taken on January 31, 2002.

MATERIALS

(b)(4) Test Data

[redacted]

(b)(4)

(b)(4) Test Data

(b)(4)

(b)(4) Test Data

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ere

(b)(4) Test Data

(b)(4)

[redacted]

APPENDIX I

ISO VAGINAL IRRITATION STUDY IN THE RABBIT (REPEATED EXPOSURE)
MICROSCOPIC EVALUATION

(b)(4) Test Data

[redacted]

(b)(4)

[redacted]

APPENDIX 1 (continued)

ISO VAGINAL IRRITATION STUDY IN THE RABBIT (REPEATED EXPOSURE)
MICROSCOPIC EVALUATION

(b)(4) Test Data

[redacted]

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Reference

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Martindale the extra pharmacopoeia 31st edition P1320-1322 & P1324

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Pharmacokinetics of Local Anaesthetics continued

3 Kanto J. Obstetric analgesia: clinical pharmacokinetic considerations. *Clin Pharmacokinet* 1986; **11**: 283–98.

4 Tucker GT. Pharmacokinetics of local anaesthetics. *Br J Anaesth* 1986; **58**: 717–31.

5 Burm AGL. Clinical pharmacokinetics of epidural and spinal anaesthesia. *Clin Pharmacokinet* 1989; **16**: 283–311.

6 Smith C. Pharmacology of local anaesthetic agents. *Br J Hosp Med* 1994; **52**: 455–60.

Uses and Administration of Local Anaesthetics

Local anaesthetics act by preventing the generation and transmission of impulses along nerve fibres and at nerve endings; depolarisation and ion-exchange are inhibited. The effects are reversible. The anaesthetic base must penetrate the lipoprotein nerve sheath before it can act and therefore agents with high lipid-solubility tend to have a greater potency and duration of action and a faster onset than agents with low lipid-solubility. Also as only unionised base can penetrate nerve membranes, the lower the pK_a of the agent the better. In general, loss of pain (analgesia) occurs before loss of sensory and autonomic function (anaesthesia) and loss of motor function (paralysis), but this may depend on the drug used and the site of administration. The effectiveness of an anaesthetic depends on the concentration attained at the nerve fibre. The latent period before the onset of action may also vary according to the concentration used and the method of administration.

Local anaesthetics are generally administered as acidic solutions of the water-soluble hydrochloride salts; alkalinisation of these solutions may increase the speed of onset and reduce the pain associated with injection (see below). Formulations employing the carbonated base rather than the hydrochloride have also been used to increase the speed of onset (see below). When adrenaline is added, a solution of about pH 3 to 5 is necessary to ensure stability.

Local anaesthetics may be administered in many different ways, some compounds being more suitable than others for a particular route of administration. The agents described in this chapter vary in their anaesthetic potency and speed of onset and duration of action; the most protein-bound agents tend to have the longest duration of action (see Table 2).

The smallest effective dose and the lowest effective concentration should be used. Smaller doses are usually needed in the elderly, in children, in debilitated patients, and in cardiac disease. Doses should also be reduced in the presence of hepatic disease. Meticulous attention to technique is essential particularly in nerve block and spinal procedures. Injections for central nerve block, such as epidural or caudal block, and spinal anaesthesia should not contain preservatives.

For certain procedures the duration of action is sometimes prolonged by the addition of a vasoconstrictor and solutions containing adrenaline 1 in 200 000 are generally advocated. Higher concentrations such as 1 in 80 000 may be used in dentistry where the total dose is small. Other vasoconstrictors including noradrenaline are also used. The total amount of adrenaline injected should not exceed 500 µg although the amount of adrenaline absorbed varies considerably with the site of administration; some consider that the maximum dose should be 200 µg.

Local anaesthetics are employed in several techniques described below. Table 3 lists the agents used in these procedures. For details of the use of local anaesthetics in the management of pain, see p.3.

Surface or **topical anaesthesia** blocks the sensory nerve endings in the skin or mucous membranes, but to reach these structures the drug must have good powers of penetration. Many of the local anaesthetics are effective surface anaesthetics, a notable exception being procaine hydrochloride. There are a number of special uses of topical anaesthesia including anaesthetising the cornea during ophthalmological procedures and the throat and larynx before intubation and bronchoscopy. Great care is necessary when employing local anaesthetics to anaesthetise the urethra; if trauma has occurred, rapid absorption of the drug may occur and give rise to serious adverse effects. Absorption from the respiratory tract is also rapid and care is essential to avoid administering a toxic dose.

Infiltration anaesthesia is produced by injection of an anaesthetic agent into and around the field of operation. In *field block* anaesthesia sensory nerve paths are blocked by subcutaneous injection of local anaesthetic close to nerves around the area to be anaesthetised. The drug must not be absorbed too rapidly otherwise the anaesthesia will wear off too quickly for practical use; some local anaesthetics require the addition of a vasoconstrictor, such as a small amount of adrenaline. If adrenaline is added to such drugs a larger total dose may be given. Infiltration anaesthesia is extensively used in dentistry.

Regional nerve block anaesthesia may include peripheral nerve block, sympathetic nerve block, and central nerve block. For a discussion of the use of nerve blocks in the management of pain, see p.5. *Peripheral nerve block* anaesthesia involves injection into or around a peripheral nerve or plexus supplying the part to be anaesthetised; motor fibres may be blocked as well as sensory fibres. Examples of this type of block include brachial plexus block, intercostal nerve block, paracervical block, and pudendal block. Adrenaline is often added as a vasoconstrictor but it must not be used when producing a nerve block in an appendage, as gangrene may occur. *Sympathetic nerve block* such as stellate ganglion blockade and lumbar sympathectomy is used in the management of a range of painful conditions and vascular diseases. For further details see under Sympathetic Pain Syndromes on p.10. Temporary block is obtained using local anaesthetics such as lignocaine or bupivacaine but permanent block may be produced with use of neurolytic agents such as phenol (see p.1141) or alcohol (see p.1115).

Central nerve block includes epidural and spinal block. *Epidural block* (also referred to as *extradural* or *peridural block*) is used to provide analgesia or anaesthesia in surgical and obstetric procedures by injecting the local anaesthetic alone or with a small dose of an opioid analgesic into the epidural space. Introduction of a cannula into the epidural space enables prolonged analgesia or anaesthesia to be provided through the use of 'top-up' doses or continuous infusion of the agents. In obstetrics the injection is made in the lumbar region in order to block the roots of sensory nerves supplying the uterus and lower birth canal. In *caudal block* an epidural injection is made through the sacral hiatus. A test dose at the intended injection site is recommended before starting epidural anaesthesia to ensure that the main dose is not injected intravascularly or into the subarachnoid space.

Spinal block (also referred to as *subarachnoid* or *intrathecal block*) is produced by injecting a solution of a suitable drug within the spinal subarachnoid space, causing temporary paralysis of the nerves with which it comes into contact. Vasoconstrictors have been added to prolong the duration of the block but the effect may not be clinically useful and there is the danger of restricting the blood supply to the spinal cord. The somatic level at which anaesthesia occurs depends on many factors including the specific gravity or baricity of the anaesthetic solution used and the positioning of the patient.

Intravenous regional anaesthesia *(Bier's block)* involves a dilute solution of local anaesthetic being injected into a suitable limb vein after exsanguination and application of a tourniquet, in order to produce anaesthesia distal to it. Arterial flow must remain occluded for at least 20 minutes after injection and adrenaline should not be used.

Intravenous analgesia involves local anaesthetics such as lignocaine being injected by continuous infusion to produce a general analgesia but the technique is potentially dangerous and seldom employed.

Table 2. Characteristics of local anaesthetics.

Type of local anaesthetic	Onset	Duration	Protein binding (%)	Relative anaesthetic potency
Amide type				
Bupivacaine	moderate to slow	long	95	8
Etidocaine	fast	long	95	4 to 6
Lignocaine	fast	intermediate	66	2
Mepivacaine	fast	intermediate	78	2
Prilocaine	fast	intermediate	55	2
Ester type				
Amethocaine	slow	long	76	8 to 10
Chloroprocaine	fast	short	rapidly hydrolysed	1 to 2
Procaine	slow	short	6	1

Action. CARBONATED SOLUTIONS. The use of carbonated solutions of local anaesthetics instead of the usual hydrochloride salts has been discussed in several reviews.[1-3] Although some early studies indicated that carbonated solutions of bupivacaine, lignocaine, or prilocaine produced earlier onset of anaesthesia and improved the quality of epidural or brachial plexus blocks not all subsequent studies have confirmed these results. A method for preparing carbonated solutions has been given by Bromage[4] but proprietary preparations of such solutions of bupivacaine or lignocaine may be available in some countries.

1. Covino BG. Pharmacology of local anaesthetic agents. *Br J Anaesth* 1986; **58**: 701–16.
2. Burm AGL. Clinical pharmacokinetics of epidural and spinal anaesthesia. *Clin Pharmacokinet* 1989; **16**: 283–311.
3. Carrie LES. Extradural, spinal or combined block for obstetric surgical anaesthesia. *Br J Anaesth* 1990; **65**: 225–33.
4. Bromage PR. Improved conduction blockade in surgery and obstetrics: carbonated local anesthetics. *Can Med Assoc J* 1967; **97**: 1377–84.

PH OF SOLUTIONS. The pain associated with infiltration of local anaesthetics can be reduced by buffering the solution to physiological pH with sodium bicarbonate.[1,2] Although buffering itself does not appear to compromise the efficacy of anaesthesia[2] alkalinisation of the solution may reduce the solubility of the local anaesthetic and cause precipitation.[2,4] To enhance stability local anaesthetic solutions are usually prepared to have an acidic pH and it is therefore recommended that buffered solutions are used immediately.[2]

Similar pH adjustments for solutions for intravenous regional anaesthesia have been reported to reduce the amount of local venous irritation and thrombophlebitis[5] and to increase the speed of onset and the duration of the block.[6] Alkalinisation of a solution used for epidural block for caesarean section has been reported to result in a more rapid onset of action and

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Table 3. Uses of local anaesthetics.

	Surface		Infiltration	Peripheral Nerve Block	Epidural Block	Spinal Block	Intravenous Regional
	Eye	General					
Amethocaine	X	X				X	
Amylocaine		X					
Benzocaine		X					
Bucricaine	X		X	X		X	
Bupivacaine			X	X	X	X	
Butacaine		X					
Butanilicaine			X	X			
Butoxycaine		X					
Butyl Aminobenzoate		X					
Carticaine			X	X		X	
Chloroprocaine			X	X	X		
Cinchocaine		X				X	
Clibucaine		X					
[illegible]rmecaine		X					
Cocaine	X	X					
Cyclomethycaine		X					
Dimethisoquin		X					
Diperodon		X					
Dyclocaine		X					
Ethyl Chloride		X					
Etidocaine			X	X	X		
Hexylcaine		X					
Isobutamben		X					
Ketocaine		X					
Lignocaine	X	X	X	X	X	X	X
Mepivacaine			X	X	X	X	
Meprylcaine			X				
Myrtecaine		X					
Octacaine		X					
[illegible]ethazaine		X					
[illegible]ybuprocaine	X	X					
Parethoxycaine		X					
Pramoxine		X					
Prilocaine		X	X	X	X		X
Procaine			X	X		X	
Propanocaine		X					
Propipocaine		X					
Propoxycaine			X	X			
Proxymetacaine	X						
Ropivacaine			X	X			

Alkalinisation has also been used to hasten the onset of peripheral nerve block[8] by increasing the proportion of the lipid-soluble nonionised free base but the effect in epidural block has been inconsistent.[9,10]

1. McKay W, *et al.* Sodium bicarbonate attenuates pain on skin infiltration with lidocaine, with or without epinephrine. *Anesth Analg* 1987; **66**: 572–4.
2. Cristoph RA, *et al.* Pain reduction in local anesthetic administration through pH buffering. *Ann Emerg Med* 1988; **17**: 117–20.
3. Bourget P, *et al.* Factors influencing precipitation of pH-adjusted bupivacaine solutions. *J Clin Pharm Ther* 1990; **15**: 197–204.
4. Nakano NI. Temperature-dependent aqueous solubilities of lidocaine, mepivacaine, and bupivacaine. *J Pharm Sci* 1979; **68**: 667–8.
5. Yudenfreund SM, *et al.* pH-Buffered 2-chloroprocaine for intravenous regional anesthesia. *DICP Ann Pharmacother* 1989; **23**: 614–15.
6. Armstrong P, *et al.* Effect of alkalinization of prilocaine on IV regional anaesthesia. *Br J Anaesth* 1989; **63**: 625P–626P.
7. [illegible]es HM. Comparison of plain and alkalinized local anaesthetic mixtures of lignocaine and bupivacaine for elective extradural caesarean section. *Br J Anaesth* 1991; **67**: 699–703.
8. Coventry DM, Todd JG. Alkalinization of bupivacaine for sciatic nerve blockade. *Br J Anaesth* 1989; **62**: 227P.
9. Burm AGL. Clinical pharmacokinetics of epidural and spinal anaesthesia. *Clin Pharmacokinet* 1989; **16**: 283–311.
10. Carrie LES. Extradural, spinal or combined block for obstetric surgical anaesthesia. *Br J Anaesth* 1990; **65**: 225–33.

VASOACTIVITY The intrinsic vasoactivity of a local anaesthetic can influence its rate of removal from the site of action and therefore its duration of action. Ester-type local anaesthetics such as amethocaine and procaine are more likely to produce vasodilatation than amide-type local anaesthetics such as cinchocaine, lignocaine, mepivacaine, and prilocaine following intradermal administration.[1] The amide-type local anaesthetics can produce vasoconstriction but apart from prilocaine their vasoconstrictor activity has generally been found to decline with increasing concentration[1,2] and in one study lignocaine and bupivacaine produced more vasodilatation than vasoconstriction at the higher concentrations tested.[2] Mepivacaine has produced greater and more consistent vasoconstriction than lignocaine, cinchocaine, or prilocaine following intradermal injection[1] but this greater vasoactivity is not always evident.[3]

1. Willatts DG, Reynolds F. Comparison of the vasoactivity of amide and ester local anaesthetics: an intradermal study. *Br J Anaesth* 1985; **57**: 1006–11.
2. Aps C, Reynolds F. The effect of concentration on vasoactivity of bupivacaine and lignocaine. *Br J Anaesth* 1976; **48**: 1171–4.
3. Goebel WM, *et al.* Comparative circulatory levels of 2 per cent mepivacaine and 2 per cent lignocaine. *Br Dent J* 1980; **148**: 261–4.

Anaesthesia of the skin. Skin anaesthesia may be carried out by dermal infiltration using an intracutaneous injection of local anaesthetic.[1] Lignocaine is commonly used to provide anaesthesia of intermediate duration while procaine has been used for short procedures and bupivacaine for a longer effect.

Formerly preparations of local anaesthetics were without effect when applied to intact skin. Attempts to achieve percutaneous anaesthesia by incorporating local anaesthetics into preparations in high concentrations or with penetration enhancers such as dimethyl sulphoxide were associated with adverse effects. However, preparations using low concentrations of local anaesthetics are now available that can produce effective percutaneous anaesthesia.

Local anaesthetics have been included in topical preparations to relieve the pain of haemorrhoids (see p.1195) but good evidence of their efficacy is lacking. Similar uses include pain relief in pruritus ani and anal fissure. Local anaesthetics used for these purposes have included lignocaine, amethocaine, cinchocaine, and pramoxine. Excessive application to the rectal mucosa should be avoided as absorption can occur and use for periods of no longer than 2 weeks is recommended to prevent sensitisation.

1. Woolfson AD, McCafferty DF. Local anaesthesia of the skin. *J Clin Pharm Ther* 1989; **14**: 103–9.

Central block. See under Epidural Block and Spinal Block, below.

Cough. Management of unproductive cough is generally aimed at treating the underlying cause (see p.1059), but there are occasions when symptomatic treatment with a cough suppressant is warranted. Local anaesthetics are among the peripherally acting cough suppressants that have been used as an alternative to the more conventional centrally acting drugs. Drugs such as lignocaine or bupivacaine have been administered by inhalation in severe intractable cough,[1-4] including cough caused by malignant neoplasms. Cough suppression is produced by an indirect peripheral action on sensory receptors, but as all protective pulmonary reflexes may be lost and bronchospasm may be induced, nebulised local anaesthetics should be used in controlled circumstances; there may also be temporary loss of the swallowing reflex.

1. Howard P, *et al.* Lignocaine aerosol and persistent cough. *Br J Dis Chest* 1977; **71**: 19–24.
2. Stewart CJ, Coady TJ. Suppression of intractable cough. *Br Med J* 1977; **i**: 1660–1.
3. Sanders RV, Kirkpatrick MB. Prolonged suppression of cough after inhalation of lidocaine in a patient with sarcoid. *JAMA* 1984; **252**: 2456–7.
4. Brown RC, Turton CWG. Cough and angiotensin converting enzyme inhibition. *Br Med J* 1988; **296**: 1741.

Endoscopy. Local anaesthetics such as lignocaine are sometimes used before endoscopy to improve patient comfort and facilitate passage of the endoscope. As mentioned in the discussion on agents used in endoscopy (see p.1251) some consider that the use of local anaesthetics for procedures such as gastro-intestinal endoscopy should probably be reserved for those patients who prefer to undergo endoscopy without sedation as their use in addition to premedication with opioids or benzodiazepines appears to serve little purpose.

Epidural block. The onset, intensity, and duration of epidural block appear to be affected by the dose and concentration of the local anaesthetic used. Various methods including alkalinisation and carbonation of the local anaesthetic solution have been used to hasten the onset of the block (see above

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Uses and Administration of Local Anaesthetics continued

under Action). One of the major applications of epidural block is in obstetrics, see p.7. The use of epidural blocks is also discussed below under Spinal Block where the merits of each form of block are considered.

CAUDAL BLOCK. Caudal block is indicated in procedures requiring block of the sacral nerves. It was once widely used for relief of pain in labour (see p.7) but has now largely been superseded by lumbar epidural block. It is routinely used to provide postoperative analgesia after lower-abdominal and urogenital surgical procedures such as hernia repair, haemorrhoidectomy, circumcision, and orchidopexy.[1] Caudal block is easier to perform in children and there appears to be a linear relationship between the spread of the block and the age of the child.[2] Agents such as opioid analgesics[3] or ketamine[4] have been added to the local anaesthetic in an attempt to increase efficacy. Caudal block has been used to provide anaesthesia for preterm babies undergoing surgical treatment of inguinal hernia[5] when it was considered to be a useful alternative to spinal anaesthesia since it is longer lasting and provides postoperative analgesia.

Continuous caudal infusion of local anaesthetic has been used to relieve ischaemia of the lower extremities in a child with meningococcaemia.[6]

1. Commission on the provision of surgical services. *Report of the working party on pain after surgery.* London: Royal College of Surgeons of England and College of Anaesthetists, 1990.
2. Schulte-Steinberg O, Rahlfs VW. Spread of extradural analgesia following caudal injection in children: a statistical study. *Br J Anaesth* 1977; **49:** 1027–34.
3. Wolf AR, *et al.* Postoperative analgesia after paediatric orchidopexy: evaluation of a bupivacaine-morphine mixture. *Br J Anaesth* 1990; **64:** 430–5.
4. Naguib M, *et al.* Ketamine for caudal analgesia in children: comparison with caudal bupivacaine. *Br J Anaesth* 1991; **67:** 559–64.
5. Gallagher TM. Regional anaesthesia for surgical treatment of inguinal hernia in preterm babies. *Arch Dis Child* 1993; **69:** 623–4.
6. Tobias JD, *et al.* Use of continuous caudal block to relieve lower-extremity ischemia caused by vasculitis in a child with meningococcemia. *J Pediatr* 1989; **115:** 1019–21.

Headache. Lignocaine has been tried intravenously and intranasally in the treatment of headache including migraine, but it has not compared well with other treatment (see p.1335); the usual treatment of headache is discussed on p.479.

Infiltration anaesthesia. Local infiltration of a local anaesthetic compared favourably with intravenous regional anaesthesia for manipulation of Colles' fractures in terms of satisfactory anaesthesia, ease and speed of performance, and lack of complications.[1] However, pain scores were higher in those patients receiving local infiltration.

Dermal infiltration is discussed briefly under Anaesthesia of the Skin p.1321.

1. Cobb AG, Houghton GR. Local anaesthetic infiltration versus Bier's block for Colles' fractures. *Br Med J* 1985; **291:** 1683–4.

DENTAL ANAESTHESIA. References to the use of intraligamental injection of local anaesthetics into the periodontal membrane for dental anaesthesia.

1. Faulkner RK. The high-pressure periodontal ligament injection. *Br Dent J* 1983; **154:** 103–5.
2. Allan DN. Administration of local anaesthetics via the periodontal membrane. *Br Dent J* 1983; **154:** 161.
3. Dhanji AR. Administration of local anaesthetics via the periodontal membrane. *Br Dent J* 1983; **154:** 161–2.
4. Bishop C. Administration of local anaesthetics via the periodontal membrane. *Br Dent J* 1983; **154:** 195.
5. Cowan A. Administration of local anaesthetics via the periodontal membrane. *Br Dent J* 1983; **154:** 278.
6. Matthews RW, Stables DK. Intraligamentary dental analgesia by dental therapists. *Br Dent J* 1985; **159:** 329–30.
7. Gray RJM, et al. Periodontal ligament injection: with or without a vasoconstrictor? *Br Dent J* 1987; **162:** 263–5.

Intravenous regional anaesthesia. Intravenous regional anaesthesia has been used for manipulation of fractures and minor surgical procedures of the limbs and when properly conducted is considered to be a simple and safe method of anaesthesia.[1] Complications can develop when this technique is employed by those without adequate knowledge and training.[1,2] Fatalities have occurred with bupivacaine.[3] As all local anaesthetics have the potential to produce convulsions and cardiotoxicity it is recommended that an anaesthetist be present with resuscitation facilities; patients should also be fasted.[1,2]

1. Armstrong P, *et al.* Anaesthesia and Colles' fractures. *Br Med J* 1990; **300:** 261.
2. Goold JE. Intravenous regional anaesthesia. *Br J Hosp Med* 1985; **33:** 335–40.
3. Heath ML. Deaths after intravenous regional anaesthesia. *Br Med J* 1982; **285:** 913–14.

Pain. The general management of pain is discussed on p.3. Local anaesthetics are used in a variety of situations for the management of pain. They are usually given by local injection or applied topically but are sometimes used intravenously in techniques such as intravenous regional anaesthesia (see above on p.1322); some local anaesthetics such as lignocaine have also been tried intravenously in the control of various chronic pain syndromes (see under Antiepileptics: Analgesics and Analgesic Adjuvants on p.4). Further mentions of the use of local anaesthetics can be found under the sections on Nerve Blocks (p.5), Rubefacients and Topical Analgesics (p.5), Cancer Pain (p.5), Diabetic Neuropathy (p.6), Labour (p.7), Musculoskeletal and Joint Disorders (p.10), Pain in Infants and Children (p.8), Postherpetic Neuralgia (p.9), Postoperative Pain (p.9), Sympathetic Pain Syndromes (p.10), and Mouth Ulceration (p.1197). See also under Anaesthesia of the Skin (above) and Headache (above).

Stings. Local infiltration or nerve block with lignocaine has been used for the relief of pain associated with stings from venomous fish[1] but bupivacaine may be preferred because it has a longer duration of action.[2] Topical application of lignocaine appears to be ineffective for jelly-fish stings[3].

1. Dormon FM. Local nerve block after stingray injury. *Lancet* 1985; **ii:** 1131–2.
2. Sutherland SK. Weever fish sting. *Med J Aust* 1984; **140:** 503–4.
3. Williamson JA, *et al.* Acute management of serious envenomation by box-jellyfish (Chironex fleckeri). *Med J Aust* 1984; **141:** 851–3.

Paracervical block. As mentioned in the discussion of the management of labour pain on p.7, the technique of paracervical local anaesthetic block has largely fallen out of favour because of the high incidence of foetal arrhythmias, acidosis, and asphyxia and isolated reports of foetal death. However, it is still used in some centres, usually when other techniques are unavailable or are contra-indicated.

Spasticity. The management of spasticity involves physiotherapy together with the use of antispastic agents (see p.1513). There is no consensus on the antispastic drug of first choice but baclofen, dantrolene, and diazepam appear to be most often used. Other approaches to treatment include nerve blocks with local anaesthetics; these can improve spasticity but should generally only be used when further muscle relaxation would not increase disability.

Spinal block. Spinal anaesthesia is obtained by injecting a local anaesthetic into the CSF in the subarachnoid space. It is best suited for surgery below the level of the umbilicus as higher blocks are likely to cause unacceptable adverse cardiovascular and respiratory effects.[1]

The advantages and disadvantages of spinal block over epidural block have been discussed both for general[2] and obstetric surgical[3,4] patients. For further references to spinal block in labour, see p.7.

Spinal block, especially in the sacral segments provides more rapid onset of surgical anaesthesia than epidural block and, although there may be difficulty in extending or limiting a spinal block, unlike epidural block patchiness of anaesthesia is most unusual.[3] Toxicity is less likely to occur with spinal block as only small doses are required.[3] However, spinal block has a greater tendency to produce hypotension and is associated with a higher incidence of headache, due to leakage of cerebrospinal fluid following injection through the dura mater; both of these effects are more common in pregnant patients.[3,4] Since spinal anaesthesia can produce considerable haemodynamic changes it is best avoided in patients with cardiac disease.[5] There is no evidence that epidural or spinal anaesthesia is a better choice for the infant in obstetric anaesthesia.[4] In the elderly, spinal block produces a lower incidence of headache than in younger patients and may be easier to perform and more reliable than epidural block.[6]

Spinal anaesthesia has been used for surgical treatment of inguinal hernia in preterm babies;[7] it is considered by some[7] to have the advantages of causing minimal physiological disturbance, avoiding the risk of general anaesthesia, and allowing prompt return to pre-operative feeding schedules but is of shorter duration than a caudal block.

Spinal and epidural blocks have been used together to obtain the rapid onset and the density of spinal block together with the ability to extend the block and provide postoperative analgesia by use of an epidural catheter.[3,4] However, an unacceptably high block has been reported in a patient who received a spinal block after an epidural block could not be extended sufficiently for caesarean section.[8] Epidural block has usually been preferred to spinal block when administration via a catheter is required on the grounds that use of a catheter in the subarachnoid space might result in more infections and produce an unacceptable incidence of headache.[3] However, the risk of infection appears to have been overestimated[3] and the incidence of headache might be reduced by using microcatheters.[9]

Local anaesthetics and opioid analgesics used together may enhance the quality of spinal anaesthesia and permit the use of lower doses.[4] Other agents such as clonidine have also been tried.[10]

Comparison of the efficacy of local anaesthetic preparations for spinal block is difficult as quality and spread of anaesthesia may be influenced by a large number of factors including the vertebral space used for injection, the posture of the patient, pregnancy, and obesity. Also the duration of action may be affected by the dose and the concomitant use of a vasoconstrictor. However, it appears generally that anaesthesia produced by lignocaine is more rapid in onset but of shorter duration than that produced by bupivacaine. Hyperbaric solutions produce higher blocks than isobaric solutions but have a shorter duration of action, and posture has little effect on the spread of isobaric solutions but is important when hyperbaric solutions are used.[1] For short procedures a 5% hyperbaric lignocaine solution provides reliable anaesthesia but lower concentrations or isobaric solutions may produce inconsistent blockade. Injection of 1.8 mL (90 mg) will allow lower limb and perineal procedures lasting up to 60 minutes. Use of 3 mL (15 mg) of a 0.5% isobaric bupivacaine solution provides a lower limb block for about 200 minutes. For a midthoracic block injection of 3 mL (15 mg) of a 0.5% hyperbaric solution of bupivacaine produces a block for 120 to 180 minutes; use of 20 mg as a 0.5 or 0.75% solution offers no advantage.[1] Smaller doses are usually needed during pregnancy[2] and 2.5 mL (12.5 mg) of 0.5% hyperbaric bupivacaine will provide satisfactory anaesthesia for caesarean section.[1,4]

1. Casey WF. Which spinal anaesthetic? *Br J Hosp Med* 1988; **40:** 425.
2. Wildsmith JAW. Intrathecal or extradural: which approach for surgery? *Br J Anaesth* 1987; **59:** 397–8.
3. Carrie LES. Extradural, spinal or combined block for obstetric surgical anaesthesia. *Br J Anaesth* 1990; **65:** 225–33.
4. Kestin IG. Spinal anaesthesia in obstetrics. *Br J Anaesth* 1991; **66:** 596–607.
5. Sullivan JM, Ramanathan KB. Management of medical problems in pregnancy—severe cardiac disease. *N Engl J Med* 1985; **313:** 304–9.
6. Ward RM, Hutton P. Factors modifying the use of anaesthetic drugs in the elderly. *Br Med Bull* 1990; **46:** 156–68.
7. Gallagher TM. Regional anaesthesia for surgical treatment of inguinal hernia in preterm babies. *Arch Dis Child* 1993; **69:** 623–4.
8. Stone PA, *et al.* Complications of spinal anaesthesia following extradural block for caesarean section. *Br J Anaesth* 1989; **62:** 335–7.
9. Benedetti C, Tiengo M. Continuous subarachnoid analgesia in labour. *Lancet* 1990; **335:** 225.
10. Bonnet F, *et al.* Prevention of tourniquet pain by spinal isobaric bupivacaine with clonidine. *Br J Anaesth* 1989; **63:** 93–6.

Surface anaesthesia. For a discussion of the use of local anaesthetics for surface anaesthesia of the skin and mucosal surfaces, see under Anaesthesia of the Skin, above.

Surgical procedures. For details of the use of local anaesthetics in the management of surgical and postoperative pain, see p.9 and under Pain in Infants and Children, p.8.

OPHTHALMIC SURGERY. Techniques used to achieve local anaesthesia for ophthalmic surgery include administering a portion of the local anaesthetic by retrobulbar injection; some is used for block of the facial nerve, and the rest is used to induce paralysis of the eyelids. A mixture of equal parts of bupivacaine 0.5% and lignocaine 2% solutions may be useful.[1] Addition of hyaluronidase to the local anaesthetic may increase the success rate for obtaining complete ocular akinesia and anaesthesia.[2]

Adrenaline, usually in a concentration of 1 in 200 000, is commonly included to prolong the duration and increase the extent of the block unless contra-indicated by the presence of orbital vascular pathology.[3]

Because of the complications associated with retrobulbar injection, other methods of local anaesthesia have been tried including peribulbar injection and injection into sub-Tenon's space;[3,4] some prefer to induce anaesthesia by subconjunctival injection of bupivacaine 0.5%[5] or lignocaine 2%[6,7] sometimes in conjunction with eye drops such as amethocaine 1% but the degree of akinesia achieved may be inferior[7] to that from retrobulbar injection.

Injections of local anaesthetics in or around the eye can themselves be painful and topical application of a cream containing a eutectic mixture of lignocaine and prilocaine has been used to alleviate any pain associated with these procedures.[8]

The use of local anaesthetics appears to prevent the endocrine and metabolic response to the stress of ophthalmic surgery when the surgery is carried out under local anaesthesia alone[9,10] but an increase in serum-cortisol concentration has been observed in the postoperative period in patients whose ophthalmic surgery had been carried out under a combination of general and local anaesthesia.[10] The efficacy of local anaesthetics in reducing increases in intra-ocular pressure induced by intubation is unclear (see under Anaesthesia on p.1511).

1. Oji E, Oji A. Bupivacaine and lignocaine for ophthalmic surgery. *Br J Ophthalmol* 1987; **71:** 86–8.
2. Thomson J. Addition of hyaluronidase to lignocaine with adrenaline for retrobulbar anaesthesia in the surgery of senile cataract. *Br J Ophthalmol* 1988; **72:** 700–2.
3. Hamilton RC. Techniques of orbital regional anaesthesia. *Br J Anaesth* 1995; **75:** 88–92.
4. Berry CB, Murphy PM. Regional anaesthesia for cataract surgery. *Br J Hosp Med* 1993; **49:** 689–701.
5. Redmond RM, Dallas NL. Extracapsular cataract extraction under local anaesthesia without retrobulbar injection. *Br J Ophthalmol* 1990; **74:** 203–4.
6. Smith R. Cataract extraction without retrobulbar anaesthetic or sedation. *Br J Ophthalmol* 1990; **74:** 205–[illegible].
7. Khoo CY. Local anaesthesia without retrobulbar injection. *Br J Ophthalmol* 1990; **74:** 639.

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Amylocaine Hydrochloride continued

arations for application to the skin or mucous membranes. It has also been used in preparations for the relief of painful anorectal conditions and has been included in oral mixtures for the relief of coughs.

The general actions of local anaesthetics are described on p.1317.

Preparations

Names of preparations are listed below; details are given in Part 3.

Proprietary Preparations

Multi-ingredient preparations. *Belg.:* Babygencal; Dentophar; Dequalinium; Glottyl†; Rectovasol; Tablettes pour la Gorge Medica†; *Canad.:* Rhino-Mex†; *Fr.:* Anolan; Arpha†; Artralgon†; Avenoc†; Biphédrine Aqueuse; Bronchodermine; Bucçawalter; Campho-Pneumine; Chloridia; Collustan; Dolodent; Élénol; Eucalyptospirine bébé†; Eucalyptospirine†; Frazoline; Glottyl; Humex; Hyalurectal†; Kaviase†; Migralgine; Otomide; Parkipan; Pastilles M.B.C†; Phléboïdine†; Pholcones; Pommade Midy†; Pulmoll; Sterlane†; Stovalone†; Stovédrine†; Suppositoires Midy†; Tieucaly†; *Ital.:* Dentinale; Proctosedyl; Rinoleina Adulti†; *Mon.:* Anusarine†; *Spain:* Emoform Aqua†; Faringesic; Hemodren Compuesto; Sanovox; *Switz.:* Stix.

Benzocaine (7608-w)

Benzocaine *(BAN, rINN).*

Anaesthesinum; Anesthamine; Benzocainum; Ethoform; Éthoforme; Ethyl Aminobenzoate; Ethylis Aminobenzoas. Ethyl 4-aminobenzoate.

$C_9H_{11}NO_2$ = 165.2.

CAS — 94-09-7.

Pharmacopoeias. In *Aust., Belg., Br., Chin., Eur., Fr., Ger., Hung., Int., It., Jpn, Neth., Port., Swiss,* and *US.*

The standards of *Ph. Eur.* apply to those countries that are parties to the Convention on the Elaboration of a European Pharmacopoeia, see p.xiii.

Colourless or white crystals or a white odourless crystalline powder. M.p. 88° to 92°.

BP solubilities are: very slightly soluble in water; freely soluble in alcohol, in chloroform, and in ether. USP solubilities are: soluble 1 in 2500 of water, 1 in 5 of alcohol, 1 in 2 of chloroform, and 1 in 4 of ether; dissolves in dilute acids; soluble 1 in 30 to 50 of almond oil or olive oil. **Protect** from light. Preparations of benzocaine should be stored in airtight containers; prolonged exposure to temperatures in excess of 30° should be avoided.

Adverse Effects and Treatment

As for Local Anaesthetics, p.1317.

Hypersensitivity. The incidence of positive reactions in patients patch tested with benzocaine has ranged from 3.3 to 5.9%.[1,2] Patch testing with benzocaine has been recommended by The International Contact Dermatitis Research Group as an indicator of contact hypersensitivity to local anaesthetics. However, Beck and Holden[3] found that of 40 patients who had had positive reactions to benzocaine with amethocaine and cinchocaine 21 were not allergic to benzocaine alone.

For a discussion on hypersensitivity reactions associated with local anaesthetics, see under Adverse Effects of Local Anaesthetics, p.1318.

1. Rudzki E, Kleniewska D. The epidemiology of contact dermatitis in Poland. *Br J Dermatol* 1970; **83**: 543–5.
2. Bandmann H-J, *et al.* Dermatitis from applied medicaments. *Arch Dermatol* 1972; **106**: 335–7.
3. Beck MH, Holden A. Benzocaine—an unsatisfactory indicator of topical local anaesthetic sensitization for the UK. *Br J Dermatol* 1988; **118**: 91–4

Precautions

As for Local Anaesthetics, p.1319.

Pharmacokinetics

See under Local Anaesthetics, p.1319.

Uses and Administration

As for Local Anaesthetics, p.1320.

Benzocaine is a surface anaesthetic of the ester type with low systemic toxicity. It is used, often in combination with other drugs such as analgesics, antiseptics, antibacterial and antifungal agents, and antipruritics, for the temporary local relief of pain associated with dental conditions, sore throats, haemorrhoids, anal pruritus and ear pain. It has also been used for pain relief in minor cuts, scrapes, burns, and sunburn, and muscular pains, strains, and sprains.

Lozenges containing benzocaine in usual doses of up to 10 mg are dissolved slowly in the mouth for the relief of sore throat. They should not be used as self-medication for longer than 5 days. Gels, pastes, solutions, and sprays containing benzocaine in concentrations of up to 20% have been used for surface anaesthesia of the mouth and throat. Benzocaine has also been used as the hydrochloride in preparations for dental pain, sore throat, and inflammatory ear disorders.

Ear drops containing benzocaine in concentrations up to 20% are used for temporary relief of ear pain. They should not be used in conditions with ear discharge or perforated tympanic membrane.

Benzocaine is used in creams, ointments, lotions, solutions, sprays, gels, and suppositories in concentrations up to 20% for topical analgesia and anaesthesia.

Obesity. It has been reported[1] that despite the inclusion of benzocaine in some over-the-counter appetite suppressants there is no good evidence of its value in obesity. The more usual strategies for the treatment of obesity are discussed on p.1544.

1. Anonymous. A nasal decongestant and a local anesthetic for weight control? *Med Lett Drugs Ther* 1979; **21**: 65–6.

Preparations

Names of preparations are listed below; details are given in Part 3.

Official Preparations

BPC 1973: Compound Benzocaine Lozenges; Compound Benzocaine Ointment;

USP 23: Antipyrine and Benzocaine Otic Solution; Antipyrine, Benzocaine, and Phenylephrine Hydrochloride Otic Solution; Benzocaine and Menthol Topical Aerosol; Benzocaine Cream; Benzocaine Gel; Benzocaine Ointment; Benzocaine Otic Solution; Benzocaine Topical Aerosol; Benzocaine Topical Solution; Benzocaine, Butamben, and Tetracaine Hydrochloride Gel; Benzocaine, Butamben, and Tetracaine Hydrochloride Ointment; Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Aerosol; Benzocaine, Butamben, and Tetracaine Hydrochloride Topical Solution.

Proprietary Preparations

Aust.: Anaestherit; *Austral.:* Applicaine; Topicaine; *Canad.:* Anbesol Baby; Teething Syrup†; Topicaine; *Ger.:* Anaesthesierende Salbe†; Anaesthesin; Flavamed Halstabletten; Subcutin N; Zahnerol N; *Ital.:* Gengivarium; *Spain:* Dentispray; Hurricaine; *Switz.:* Ora-jel; *UK:* AAA; Burneze; Lanacane; Vicks Ultra Chloraseptic; *USA:* 3 in 1 Toothache Relief; Americaine Anesthetic; Americaine Anesthetic Lubricant; Baby Anbesol; Baby Orajel; BanSmoke; Benzocol; Benzodent; Chigger-Tox; Dent's Extra Strength Toothache Gum; Dent's Lotion-Jel; Dent's Maximum Strength Toothache Drops; Dermoplast; Detane; Diet Ayds; Hurricaine; Medamint†; Mycinettes; Numzident; Orabase Baby; Orabase-B; OrabaseGel; Orajel; Oratect; SensoGARD; Slim-Mint; Spec-T; Trocaine; Unguentine; Vicks Children's Chloraseptic; Zilabrace†; Zilactin-B Medicated; ZilaDent.

Multi-ingredient preparations. *Aust.:* Dequalinetten; Dolothricin; Herposicc; Rectosan; Sulgan 99; Tyrothricin comp; *Austral.:* AAA†; Adacol†; Animine; Auralgan; Ayrton's Chilblain; Benzotol†; Cepacaine; Cepacol Anaesthetic; Cepacol Cough and Sore Throat; Codral Lozenges†; Cornkil; Dermoplast†; Le Trim-BM†; Nyal Toothache Drops; Oticane†; Rectinol; Sedaural†; *Belg.:* Hibitane; Intralgin†; Myalgesic; Nestosyl; Tablettes pour la Gorge Medica†; Transvane†; *Canad.:* Anbesol; Anivy; Antibiotic Cold Sore Ointment†; Appedrine; Auralgan; Aurisant†; Balminil Pastilles†; Bionet; Calmasol; Cepacol; Chloraseptic Sore Throat Lozenges—Cherry Flavour; Dermoplast; Dexatrim; Foille; Ivarest; Jiffy Toothache Drops; Kank-A; Lanacane; Osmopak-Plus†; Oxipor; Rectogel HC†; Rectogel†; Scabanca†; Slim Mint; Solarcaine; Spec-T†; Vagisil; Webber Antibiotic Cold Sore Ointment; ZAP; *Eire:* AAA; Aidex; Auraltone; Oxipor; Transvasin; *Fr.:* Anti-Hémorroïdaires; Nestosyl; Pommade Midy†; Sédorrhoïde; Sulforgan†; Suppositoires Midy†; *Ger.:* Anaesthesetten N†; Anaesthesin N; Anaesthesin-Rivanol; Antussan†; Anusept; Baranmild N; Claudemor†; Combustin Heilsalbe; Consablitz†; Dolexacur†; Dolexaderm†; Dolexamed†; Dolo-Dobendan; Doretonsin†; Dorex†; Dorithricin; Dr. Scheller's Hämorrhoiden-Salbe†; Duoform-Balsam†; Eulatin NN; euseptt; F 99 Sulgan; Gastripan N†; Gelum-Supp; haemo-feldhoff†; Hexoraletten N; Imposit N; Inspirol N Tablets; Larylin Husteniöser†; Lucrusanum†; Mandro-Angin†; Memento†; Neo-Facilus†; Nordapanin N; Nordathricin N; Odala wern; Rectosellan H; Risin†; Salistoperm; Spricaine Spray†; Stipo; Targophagin; Tonsilase dolo; Tubahäm†; Tyrosolvetten; Ulcerisan†; *Ital.:* Antiemorroidale Milanfarma†; Antiscabbia Candioli al D.D.T. Terapeutico; Dentosedina; Fialetta Odontalgica Dr. Knapp; Foille; Foille Plus; Golamixin; Labocaina; Lenisun; Pinselina Dr. Knapp; Pomata Midy HC; Pomata Midy†; Proctidol; Proctosedyl; Proctosoll; Supposte Midy†; Trusi†; *S.Afr.:* AAA; Auralgicin; Aurasept; Aurone Forte; Benzet; Beracal; Calasthetic; Cepacaine; Cepacol Cough Discs; Cetoxol; Covancaine; Covotop; Dermoplast†; Histamed; Intralgin; Medi-Keel A; Orochlor; Otised; Oto-Phen Forte; Rectosan 'A'; Frochain; Viodor; *Spain:* Angicola; Angitonil†; Angileptol; Anithe; Bactrocid; Bronquiolina; Cafiaspirina; Cathejo; Cetoxol; Cistitol; Cloroseptina; Colirio Kim; Colirio Ocumycin; Colirio Ocusoft; Colirio Sanitas; Colirio Tobrex; Colirio Vitamina; Colirio Vitamina A; Colirio Vitamina A-D; Colirio Vitamina A-D-E; Colirio Vitamina A-E; Colirio Vitamina D; Colirio Vitamina D-E; Colirio Vitamina E; Colirio Vitamina K; Colirio Vitamina K-D; Colirio Vitamina K-D-E; Colirio Vitamina K-E; Colirio Vitamina K-E-D; Colirio Vitamina K-E-D-A; Colirio Vitamina K-E-D-A-C; Colirio Vitamina K-E-D-A-C-B; Colirio Vitamina K-E-D-A-C-B-P; Colirio Vitamina K-E-D-A-C-B-P-Ca; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus-Uuo; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus-Uuo-Uup; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus-Uuo-Uup-Uuh; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus-Uuo-Uup-Uuh-Uus; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus-Uuo-Uup-Uuh-Uus-Uuo; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-Ti-Zr-Ag-Au-Pt-Pd-Rh-Ru-Os-Ir-Hg-Tl-Pb-Bi-Po-At-Rn-Fr-Ra-Ac-Th-Pa-U-Np-Pu-Am-Cm-Bk-Cf-Es-Fm-Md-No-Lr-Rf-Db-Sg-Bh-Hs-Mt-Ds-Rg-Cn-Uut-Uuq-Uuh-Uus-Uuo-Uup-Uuh-Uus-Uuo-Uup; Colirio Vitamina K-E-D-A-C-B-P-Ca-Mg-Fe-Zn-Cu-Mn-Se-Cr-Mo-Co-Ni-Sn-Si-V-Li-Al-Ba-Sr-

Records processed under FOIA Request #2015-4705; Released by CDRH on 3/7/2016

FDA/CDRH IMAGING SYSTEM

Page Count Discrepancy Information

The page behind page 37 was numbered page 39

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