



Use and procurement of additional lubricants for male and female condoms: WHO/UNFPA/FHI360 Advisory note

Use and procurement of additional lubricants for male and female condoms: WHO/UNFPA/FHI360 Advisory note

Introduction

The World Health Organization, Department of Reproductive Health and Research, in collaboration with United Nations Population Fund (UNFPA) and Family Health International (FHI360) convened the WHO/UNFPA/FHI Female Condom Technical Review Committee Meeting at World Health Organization, Geneva, Switzerland from 11 to 15 April 2011. Among the issues technical experts were asked to address was the question raised by Member States as to whether or not WHO could review the evidence and recommend to UNFPA the linked provision of lubricants for bulk procurement with male and female condoms.

Following discussion of the issues at the meeting, a draft position paper was circulated for review. At this stage additional experts with specialist knowledge of personal lubricants were invited to contribute to the review process. The conclusions of the review are detailed in this document.

Background

Additional lubricants, supplied separately and applied to the condom, vagina, penis or rectum at the time of intercourse, are sometimes used to improve lubrication, moistening and comfort during intercourse. These lubricants are usually referred to as personal lubricants.

Moreover, additional lubricants are also frequently used by men who have sex with men (MSM) and sex workers. In a survey of Latino MSM in New York City, 93% used additional lubricants (59% always and 74% in at least 80% of sexual encounters) regardless of condom use (1). In a survey of MSM in San Francisco 89% reported always using a lubricant (2). Female sex workers also report high rates of additional lubricant use with condoms. Sex workers in brothels in the American state of Nevada used additional water-based lubricant with condoms 89% of the time (3). These women most frequently apply the additional lubricant to the outside of the condom or the surfaces of the vagina.

Impact of additional lubricants on condom failure rates

Anal intercourse: research suggests that the use of additional water-based lubricants is particularly important for anal intercourse. In a prospective study (4), condom breakage was found to be associated with the type of additional lubricant used ($\chi^2 = 44.34$, $p < 0.0001$). When the water-based lubricant that was supplied with the study condoms was used, the breakage rate was 3% whereas it was 21.4% when no additional lubricant was used.

40 
years of innovation

UNDP · UNFPA · WHO · World Bank
Special Programme of Research, Development
and Research Training in Human Reproduction



World Health
Organization



Vaginal intercourse: evidence for the impact of additional water-based lubricant use on condom breakage and slippage rates in vaginal intercourse is equivocal. In a retrospective study (5), the use of additional water-based lubrication was associated with lower condom failure rates (odds ratio 8.88, 95% confidence interval 3.78–20.8). A further study (6) found an association between additional water-based lubricant use and reduced breakage rates for aged condoms but not for new condoms. With aged condoms¹ the breakage rate reduced from 4.5% to 2.1% ($p=0.029$). With new condoms, the breakage rate was 2.4% irrespective of additional lubricant use.

Other studies have failed to show any improvement in condom failure rates resulting from additional water-based lubricant use. For example, Smith et al. (7) in a prospective study found that additional lubricants had no effect on slippage and breakage during vaginal intercourse. However, when the additional lubricant was inserted directly into the vagina, the odds ratio for breakage reduced to 0.34 but the authors did not state whether this result was statistically significant. Sparrow and Lavill (8) also found no association between the use of additional lubricants and breakage or slippage rates, although they reported that “not enough lubrication or dryness” was cited as the second most frequent explanation for condom breakage.

What type of lubricant should be procured?

Any additional lubricant that is used must not have a deleterious effect on the properties of the condoms, such that the risk of breakage is increased.

Therefore the most important issue to consider is the type of lubricant that is used as latex condoms rapidly lose strength if exposed to oil-based lubricants. Evidence suggests that using incorrect lubricants contributes significantly to increased rates of breakage and slippage (9).

Silicone oils (polydimethylsiloxane), also known as silicone fluids, are the most commonly used lubricants that are applied to male and female condoms during manufacture. A very wide range of different silicone fluids is available but condom manufacturers generally use polydimethylsiloxanes with viscosities in the range 200–350 centistokes. Silicone fluids are inert, safe and have minimal effect on the properties of the latex film (10). They are not, however, widely available as personal lubricants in many markets. They also tend to be relatively expensive. Although silicone fluids are expected to be safe and effective when used as personal lubricants, there are currently no published clinical studies supporting their use in this role, particularly when used with latex condoms for anal intercourse.

Most widely available personal lubricants are water based, and these are commonly used as additional lubricants with condoms. Examples include K-Y Jelly, Astroglide, ID Glide and many others (see Annex 1). Many condom manufacturers also supply a range of water-based, condom-compatible lubricants.

Water-based lubricants normally contain one or more water soluble polymers to control their viscosity, together with humectants, viscosity modifiers, moisturizers and other components to modify their texture, rate of water evaporation and lubricating properties. Some lubricants are claimed to be long lasting and are marketed as vaginal moisturizers. The hydrophilic polymers used in those products are claimed to be bio-adhesive and to provide long term moisturizing effects.

Water-based lubricants must contain preservatives to prevent microbial growth. These preservatives can cause irritation and sensitization in some individuals. The most commonly used preservatives are esters of p-hydroxybenzoic acid (parabens). Other preservatives that are used include sorbic acid and sorbates, phenoxyethanol, benzoic acid, and less commonly chlorhexidine gluconate and domiphen bromide.

Other lubricants that are suitable for use with condoms are glycol based. Glycols, such as glycerol and propylene glycol, are commonly added to water-based lubricants as humectants but propylene glycol is also used as the primary component in some lubricant formulations. Warming lubricants often contain high levels of propylene glycol.

Household products are also sometimes used as personal lubricants. Some have a highly damaging effect on latex and should not be used with natural rubber latex condoms (see Table 1) (11).

Table 1

Household products that should not be used with latex condoms

Baby oil
Burn ointment
Dairy butter
Palm or coconut oil
Cooking oil
Fish oil
Mineral oil
Suntan oil
Haemorrhoid cream
Petroleum jelly (Vaseline)
Body/hand lotions

¹ The aged condoms were stored for one year.

Condom compatibility

Natural rubber latex condoms

Methods of testing additional lubricants for compatibility with condoms are being developed by technical working group 15 of the International Organization for Standardization (ISO) Technical Committee for Non-Systemic Contraceptives and STI Barrier Prophylactics (ISO/TC 157 WG 15). At present this working group has not completed its assignment because poor inter-laboratory reproducibility has delayed the development of a widely acceptable test procedure.

Water and glycol based personal lubricants, as described above, are generally accepted as being compatible with natural rubber latex and are therefore safe to use with latex condoms. Silicone oil-based lubricants are also compatible with natural rubber latex but are more expensive than water and glycol based lubricants.

Condoms made from polyurethanes and synthetic materials

Almost any lubricant with proven levels of safety for human use can be used with polyurethane condoms (12) and some other types of synthetic condoms. However, other synthetic materials now used for making condoms, such as polyisoprene, are just as sensitive to oil-based lubricants as are latex condoms. It is therefore necessary to check very carefully the material used to make the condom before using an oil-based lubricant.

Safety issues

Personal lubricants are generally regarded as low-risk products and are subjected to only limited regulatory controls. Depending upon product claims and intended duration of action, they are classified as class 1 or class 2 medical devices in the United States and subject to 510(k) premarket approval. In Europe they are classified as class I or class IIa medical devices, again depending on product claims including duration of action.

Depending on classification they can be marketed based on the manufacturer's declaration of conformity (class I) or following Notified Body review (class IIa). Safety testing is often restricted to vaginal and penile irritation/sensitization studies in the rabbit.

Recent studies have identified a number of potential safety issues with personal lubricants. Much of this new information is based on laboratory (in vitro) testing. Several papers (13–16) suggest that lubricants with high osmolality might cause vaginal and anal epithelial damage. Confirmation that lubricants with high osmolality can cause epithelium damage when applied rectally to humans has been demonstrated in a group of 10 volunteers (15).

Epithelial damage could in turn increase the risk of infection, for example by HIV and other sexually transmitted infections (STIs), particularly when condom use is inconsistent. The effect of high osmolality might be more important when these lubricants are used rectally (15).

Most commercial personal lubricants have high osmolalities (2000–6000 mOsm/kg). Table 1 summarizes data on a wide range of current commercial products (16). By comparison, the normal osmolality of female vaginal secretions is 260–290 mOsm/kg and in human semen it is 250–380 mOsm/kg (17, 18). Ideally, the osmolality of a personal lubricant should not exceed 380 mOsm/Kg to minimize any risk of epithelial damage. Given that most commercial lubricants significantly exceed this value, imposing such a limit at this time could severely limit the options for sourcing personal lubricants for sector procurement. It is therefore recommended on an interim basis that procurement agencies should source lubricants with osmolalities of not greater than 1200 mOsm/kg.

The primary factor determining the osmolality of the majority of lubricants is the concentration of glycol. Glycols are added as humectants/moisturizers. Glycerol and propylene glycol are most commonly used. To maintain osmolalities below 1200 mOsm/kg the concentration of glycerol in the formulation should not exceed 9.9% mass fraction (w/w) and the concentration of propylene glycol should not exceed 8.3% mass fraction. If a mixture of glycols is used then the total glycol content should be kept below approximately 8.3% mass fraction although the exact limit will depend upon the ratio of the glycols.

Procurement agencies might therefore want to consider requesting information about the osmolality of lubricants from the manufacturers when selecting products for bulk purchase, especially if the products could be used rectally and/or by high-risk populations. If manufacturers are unable to supply information about the osmolality of their lubricants then information about the glycol content should be requested.

In a study undertaken by Population Council (16), four lubricants (Astroglide Liquid, Astroglide Warming Liquid, Astroglide Glycerin & Paraben-Free Liquid, and Astroglide Silken Secret) significantly enhanced HIV-1 replication in vitro compared with other lubricants in the study ($p < 0.0001$). A common ingredient in all of these preparations is polyquaternium (polyquaternium-15 is specified in three of them). A related polyquaternium compound, MADQUAT, was also found to increase HIV-1 replication, suggesting that this class of compound might increase HIV infection risk.

Other researchers found that polyquaternium-32 disrupted infected leukocytes in vitro within 5 minutes, which resulted in

inhibition of infectious HIV production by infected leukocytes (19). It is not clear whether the different effects seen in these studies are due to the test methods used or differences between specific polyquaternium compounds. Until the role of polyquaternium compounds is clarified they are best avoided in personal lubricants, particularly in products intended for use by high-risk populations.

The pH of the healthy vagina is normally in the range 3.8–4.5. The pH of the rectum is closer to neutral (pH 7). High vaginal pH can lead to an increase in the risk of bacterial vaginosis. High pH is also more supportive of HIV survival. Ideally therefore a vaginal lubricant should have a pH of about 4.5 and a rectal lubricant of about 5.5 to 7. It is unfortunate that these optimum requirements cannot be bridged in a single lubricant. The preservation of water-based lubricants is easier if the pH is maintained below 7. For these reasons it is recommended that procurement agencies purchase lubricants that have a pH of 7 or less. Also, agencies should consider the primary intended target population when specifying personal lubricant requirements, and also consider the likelihood of cross over use, e.g. a lubricant designated for rectal use being used vaginally and vice versa.

In the process of developing the recommendations in this paper a review of the literature was undertaken but this was not done on a formal, systematic basis. To provide a definitive recommendation on lubricants, it is proposed that a systematic review of the literature on the safety of personal lubricants be undertaken to define both the knowledge and research gaps.

In the interim, it would seem prudent for procurement agencies purchasing personal lubricants for public sector distribution to:

- Try and limit osmolality to less than 1200 mOsm/kg (total glycol content below ca 8.3% mass fraction (w/w)).
- Avoid lubricant formulations containing polyquaternium 15 specifically, and perhaps polyquaternary compounds in general.

In addition:

- If the primary intended target population use is vaginal use then a pH of 4.5 is preferable.
- If the primary intended users are MSM or cannot be determined, then a pH in the range 5.5–7 would be more appropriate.

Careful consideration should be given to the potential risk factors particularly when procuring lubricants for HIV/STI prevention programmes and for MSM.

Adopting an upper limit of 1200 mOsm/kg will have a significant impact on the number of available commercial lubricants that can be currently procured. Most current commercial lubricants, as reported above, have osmolalities in the 2000–6000 mOsm/kg range. The formulation of low osmolal lubricants does not, however, present any significant technical challenges. There are a number of products available that meet or only just exceed the recommended limit of 1200 mOsm/kg.

Spermicidal additives

Spermicidal additives to the lubricant have been used in some commercial products. Recent summaries of research findings suggest that these spermicides (predominantly nonoxynol-9) have significant irritant effects, and, overall, **their use is not recommended** (12).

Addition of medicinal and other active substances to condom lubricants

In the commercial sector there is increasing availability of condoms containing medicinal substances such as local anaesthetics. A common example is benzocaine, which is added to delay ejaculation. Lubricants containing medicinal substances are subject to local regulatory requirements for medicines. It may not be legal to distribute them in many countries without specific local regulatory approvals. **The inclusion of such products in bulk procurement programmes is therefore not recommended.**

Personal lubricants are also available with herbal and other substances that are claimed to have specific benefits, such as stimulating, warming, tingling and other effects. Since these lubricants do not contain medicinal substances, they are not regulated as medicines. Nevertheless, the safety of such lubricants in high-risk populations such as MSM and sex workers may not have been adequately assessed to date. Again, their inclusion in bulk procurement programmes is not recommended.

Conclusion and recommendations

Based on discussions at the meeting and an extended review with additional technical experts following the meeting, the technical experts recommended that:

1. There is a significant demand for additional lubricants to be used with condoms, particularly for MSM, female sex workers and women in menopause, and post-menopause.
2. The correct type of additional lubricant for male latex and female condoms can be bulk procured with either male or female condoms, if justified by programmatic requirements.
3. When procuring water-based lubricants, the osmolality should preferably be 1200 mOsm/kg or less. This can be achieved by limiting the glycerol content of the lubricant to 9.9% mass fraction or less, the propylene content to 8.3% mass fraction or less, or if a mixture of glycols is used a total limit of ca 8.3% mass balance.
4. Lubricants containing polyquaternary compounds should be avoided until there is further evidence on the effect of polyquaternium compounds on HIV replication rates.
5. When procuring water-based lubricants, a pH of around 4.5 is recommended if the primary intended target population will use the product for vaginal intercourse. For lubricants intended primarily for MSM or where the nature of the intended use cannot be ascertained, a pH in the range 5.5 to 7 is recommended. Lubricants with pH exceeding 7 are not recommended.
6. The bulk procurement and distribution of lubricants containing spermicides, medicinal and other active substances is not recommended.
7. A formal, systematic review of the literature should be undertaken by WHO to determine the sum of evidence on which recommendations can be made for the bulk procurement and distribution of personal lubricants that can be safely used as additional lubricant with male and female condoms.

Acknowledgements

The World Health Organization Department of Reproductive Health and Research (RHR) would like to thank William Potter, Independent Consultant, Stapleford Scientific Services, Cambridge, United Kingdom; Margaret Usher-Patel, RHR Scientist/IBP Secretariat; Timothy Farley, Scientist, WHO/RHR and Catherine D'Arcangues, Deputy Director, RHR, for initiating and supporting the preparation of this paper in collaboration with the following members of the Female Condom Technical Review Committee: Mags Beksinska, Match, Tunbridge Wells, United Kingdom; Eli Carter, Family Health International 360, Durham, United States of America; John Gerofi, Enersol Consulting Engineers, Annadale, Australia; Carol Joanis, Joanis Consulting, Raleigh, United States of America; Els Klinkert, UNAIDS, Geneva, Switzerland; Twedi Seane, South African Bureau of Standards, Pretoria, South Africa; K Sivakumar, Independent Technical Adviser, Chennai, India; Jakub Srebro, JS –International Auditing & Consulting, Stockholm, Sweden; Mark Weaver, Family Health International 360, Durham, United States of America; David Whybrew, Crown Agents, Sutton, United Kingdom; Agnes Chidanyika, UNFPA, Copenhagen, Denmark; Bidia Deperthes, UNFPA, New York, United States of America; Morten Sorensen, UNFPA, Copenhagen, Denmark; Hayley Traeger, UNFPA, Copenhagen, Denmark and Mark Weaver, Family Health International 360, Durham, USA.

WHO would also like to acknowledge the scientific and technical contributions received from the key experts involved in the extensive external review process: Markus Steiner, Family Health International 360, Durham, USA; Nathalie Broutet, RHR; Francis Ndowa, RHR; David F. Katz, Duke University, Durham, USA; Marc-André LeBlanc, International Rectal Microbicide Advocates (IRMA), USA; Cheikh E Traore, United Nations Development Programme, New York, USA; Mark Rillings, Office of Population and Reproductive Health, USAID, USA; Kevin O'Reilly, Department of HIV/AIDS, WHO and Catherine Richey, RHR.

References

1. Carballo-Diéguez A, Stein Z, Sáez H, Dolezal C, Nieves-Rosa L, Díaz F. Frequent use of lubricants for anal sex among men who have sex with men: the HIV prevention potential of a microbicide gel. *American Journal of Public Health*, 2000, 90(7):1117-1121.
2. Carballo-Diéguez A, O'Sullivan LF, Lin P, Dolezal C, Pollack L, Catania J. Awareness and attitudes regarding microbicides and Nonoxynol-9 use in a probability sample of gay men. *AIDS and Behavior*, 2007, 11(2):271-276.
3. Albert AE et al. Condom used among female commercial sex workers in Nevada's legal brothels. *American Journal of Public Health*, 1995,85: 1514-1520.
4. Golombok R, Harding R, Sheldon J. An evaluation of a thicker versus standard condom with gay men. *AIDS*, 2001, 15:245-250.
5. Gabbay M, Gibbs A. Does additional lubrication reduce condom failure? *Contraception*, 1996, 53(3): 155-158.
6. Steiner M, et al. The impact of lubricants on latex condoms during vaginal intercourse. *International Journal of STD & AIDS*, 1994, 5(1): 29-36.
7. Smith AM, et al. Does additional lubrication affect condom slippage and breakage? *International Journal of STD & AIDS*, 1998, 9(6): 330-335.
8. Sparrow MJ, Lavill K. Breakage and slippage of condoms in family planning clients. *Contraception*, 1994, 50(2): 117-129.
9. Crosby R, Diclemente RJ, Yarber WL, Snow G, Troutman A. An event-specific analysis of condom breakage among African American men at risk of HIV acquisition. *Sexually Transmitted Diseases*, 35(2):174-177.
10. WHO, UNFPA, UNAIDS, FHI. *Male latex condom: specification, prequalification and guidelines for procurement 2010*. Geneva, World Health Organization, p.128.
11. Steiner MJ, Taylor D, Hylton-Kong T, et al. Decreased condom breakage and slippage rates after counseling men at a sexually transmitted infection clinic in Jamaica. *Contraception*, 2007, 75 (4):289-293.
12. Jennings P, Bachmann L. A clinician's guide to condoms, spermicides, microbicides and lubricants. *Journal of the American Academy of Physician Assistants*, 2005, 18(12):61-62, 67-69.
13. Adriaens E and Remon JP. Mucosal irritation potential of personal lubricants relates to product osmolality as detected by the slug mucosal irritation assay. *Sexually Transmitted Diseases*, 2008, 35:512-516.
14. Wang et al. Rectal microbicides: clinically relevant approach to the design of rectal specific placebo formulations. *AIDS Research and Therapy*, 2011, 8:12.
15. Fuchs EJ, Lee LA, Torbenson MS, et al. Hyperosmolar sexual lubricant causes epithelial damage in the distal colon: potential implication for HIV transmission. *Journal of Infectious Disease*, 2007; 195:703-710.
16. Begay O, Jean-Pierre N, Abraham CJ, et al. Identification of personal lubricants that can cause rectal epithelial cell damage and enhance HIV Type 1 replication in vitro. *AIDS Research and Human Retroviruses*, 2011, 27(9):1019-1024.
17. Owen DH, Katz DF. A vaginal fluid simulant. *Contraception*, 1999, 59:91-95.
18. Owen DH, Katz DF. A review of the physical and chemical properties of human semen and the formulation of a semen simulant. *Journal of Andrology*, 2005, 26:459-469.
19. Nguyen D, Lee H, Poast J, Cloyd MW, Baron S. Preventing sexual transmission of HIV: anti-HIV bioregulatory and homeostatic components of commercial sexual lubricants. *Journal of Biological Regulators & Homeostatic Agents*, 2004, 18(3-4):268-274.

Annex 1. Properties of some commercial lubricants

Lubricant	Manufacturer	Osmolality (mOsm/kg)	pH
KY Jelly	Johnson & Johnson, Langhorne, PA, USA	2007	4.55
KY Warming Jelly	Johnson & Johnson, Langhorne, PA, USA	ND	4.50–6.50
KY Tingling Jelly	Johnson & Johnson, Langhorne, PA, USA	5047	3.61
KY Sensual Silk	Johnson & Johnson, Langhorne, PA, USA	5467	3.39
KY Sensual Silk Warming	Johnson & Johnson, Langhorne, PA, USA	ND	5.00–7.00
KY Sensual Silk Tingling Ultragel	Johnson & Johnson, Langhorne, PA, USA	5381	3.36
KY Natural Feeling Liquid	Johnson & Johnson, Langhorne, PA, USA	4523	3.86
Wet Original Gel Lubricant	Trigg Laboratories, Valencia, PA, USA	3679	5.9
Wet Light	Trigg Laboratories, Valencia, PA, USA	3946	6.02
Wet Warming	Trigg Laboratories, Valencia, PA, USA	ND	6.0–7.5
Durex Play Soothing	Ssl international, London, United Kingdom	1373	4.2
Durex Play Warmer	Ssl international, London, United Kingdom	ND	4
Durex Play Piña Colada	Ssl international, London, United Kingdom	ND	4.29
Durex Play More	Ssl international, London, United Kingdom	1332	4.49
ID Glide	Westridge Laboratories Inc, Santa Ana, CA, USA	2901	5.2
ID Juicy Lube Cherry	Westridge Laboratories Inc, Santa Ana, CA, USA	3030	5.35
ID Pleasure	Westridge Laboratories Inc, Santa Ana, CA, USA	2898	5.26
ID Sensation	Westridge Laboratories Inc, Santa Ana, CA, USA	ND	5.95–6.5
Astroglide Liquid	BioFilm Inc, Vista, CA, USA	8064	4.44
Astroglide Gel	BioFilm Inc, Vista, CA, USA	2299	4.3
Astroglide Warming Liquid	BioFilm Inc, Vista, CA, USA	ND	6.45–6.73
Astroglide Glyceryn & Paraben-Free Liquid	BioFilm Inc, Vista, CA, USA	4806	4.54
Astroglide Strawberry	BioFilm Inc, Vista, CA, USA	ND	5.35
Astroglide Silken Secret	BioFilm Inc, Vista, CA, USA	6121	4.73
Lifestyles Liquid (with Aloe & Vit. E)	Ansell Limited, Richmond, Victoria, Australia	4229	6.3
Lifestyles Excite Sensual Gel	Ansell Limited, Richmond, Victoria, Australia	3728	7.2
Lifestyles Warm Lovin'	Ansell Limited, Richmond, Victoria, Australia	ND	5.24
Maximus	Bodywise Limited, Isle of Wight, United Kingdom	6415	6.05
Babelube	Babeland, Seattle, WA, USA	19	6.78
Elbow Grease Thin Gel	B. Cumming Company Inc, Sun Valley, CA, USA	2977	5.77
Slippery Stuff Gel	Wallace O'Farrell Inc, Puyallup, WA, USA	13	6.89
O'My Natural Lubricant	O'My Products Inc, Vancouver, BC, Canada	4348	5.46
Liquid Silk	Bodywise Limited, Isle of Wight, United Kingdom	3167	5.26
Probe Personal Lubricant	Darvryan Laboratories Inc, Portland, OR, USA	341	7.67
Anal Lube Original Formula	California Exotic Novelties Inc, Chino, CA, USA	3456	5.77
ForPlay Gel-Plus	Trimensa Pharmaceuticals, Newbury Park, CA, USA	9177	6.58
Gun Oil H ₂ O	Empowered Products Inc, Las Vegas, NV, USA	3955	5.61
Duane Reade Lubricating Jelly	Duane Reade Inc, New York, NY, USA	737	4.79
Moist Again Vaginal Moisturizing Gel	Lake Consumer Products Inc, Jackson, WI, USA	187	5.68
Replens	Lil' Drug Store Products Inc, Cedar Rapids, IA, USA	1491	2.98
FemGlide	Cooper Surgical Inc, Puyallup, WA, USA	15	6.13

Source: (16).

For more information, please contact:

Department of Reproductive Health and Research
World Health Organization
Avenue Appia 20, CH-1211 Geneva 27 Switzerland
Fax: +41 22 791 4171
E-mail: reproductivehealth@who.int
www.who.int/reproductivehealth

WHO/RHR/12.33

© World Health Organization 2012

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.