

Safety of lubricants for rectal use: Questions & Answers for HIV educators and advocates

Many men, women and transgender people use lubricants (lubes) during anal intercourse (AI), yet we know very little about the safety* of these products. Knowing more about lube safety is important for public health reasons. We could use this information to promote the use of safer lubes, while discouraging the use of those shown to be less safe.



What studies have been done to test the safety of lubes for rectal use?

Researchers have conducted one clinical study and a few laboratory studies to test sexual lubes. For example:

- Only one study¹ has tested the effect of lubes on rectal tissue in humans, in addition to testing these lubes in a laboratory setting. It showed that a single rectal application of a hyperosmolar rectal lube (see *Text Box 1*) can cause damage to the rectal tissue.
- Some studies² have used human tissue (taken from the vagina or rectum) and tested lubes *in vitro*[†] to see if they were toxic, irritating or caused damage to the tissue.
- Some studies^{3,4} tested lubes on rectal tissue in mice to see if they were toxic, irritating or caused damage.
- Some studies^{5,6,7,8} tested lubes in a laboratory to see if they killed HIV *in vitro*.

Most water-based lubes tested in these studies were shown to be damaging to rectal tissue. However, in the case of the first three types of studies listed above, some lubes were more damaging than others.

Another study⁹ looked at the link between the use of lubes during AI and some sexually transmitted infections (STIs) in the rectum. Women and men in two U.S. cities were asked about their use of lubes during AI, and were tested for STIs. Women and men who reported that they had used lubes during AI in the past month were more likely to test positive for a rectal STI during the study than those who reported not using lubes during AI—and this was true whether or not they had used condoms. While the study showed a strong association between using lube and having a rectal STI, it was not designed to show whether the timing of lube use and acquiring a rectal STI coincided, nor was it designed to show whether the lubes *caused* the higher rate of rectal STIs. The study also did not indicate the specific lubes used by participants.

* One way of measuring safety is through a Phase I trial (also called a safety trial): This is a small study, enrolling approximately 25-40 volunteers. To test safety for rectal use, it could assess how the lube is tolerated and check for any side effects (cell damage, inflammation, irritation). Further studies could assess whether the rectal use of lube has any effect on the risk of acquiring rectal STIs or HIV.

† *In vitro*: A Latin phrase that means “in glass,” and that refers to an artificial environment created in a laboratory test tube to study different organisms or tissues.

1: What does osmolarity have to do with lube safety?

Osmolarity is a measure of the concentration of the soluble components—or solutes—present in a solution. Products can be iso-osmolar, hypo-osmolar or hyperosmolar. Iso-osmolar products have the same osmolarity as normal cells. Hypo-osmolar products tend to make cells swell up with water, which can lead to cells bursting. Hyperosmolar products have a higher concentration of solutes than normal human cells. Therefore, when in contact with the cells of the rectum or vagina, they tend to “suck” away water from inside cells, making them shrink in size. Both hypo- and hyperosmolar products could potentially increase the risk of acquiring HIV and STIs because of their abrasive effect on the lining inside the rectum, but this assumption requires further research.

Studies^{10, 11, 12} have found that many water-based lubes are hyperosmolar, which may explain why these products tend to show greater damage to cells.



What do we know about the rectal safety of sexual lubes, based on these studies?

We still don't know exactly what laboratory tests should be used to assess lubes. Even when a study shows a specific lube causing damage in the laboratory, we don't know how that finding actually transfers to the real world. We don't know to what extent—if any—using such a lube might lead to a higher risk of acquiring HIV or STIs.

The studies mentioned above do tell us that all lubes are not created equal: a few cause little to no inflammation[‡] and cell damage, while many others have higher levels of toxicity. We have now seen this in one clinical study and a few laboratory-based studies. Given what we have learned from this handful of studies, it seems likely that osmolarity plays an important role. Lubes with higher osmolarity are associated with higher levels of inflammation and cell damage, which may explain the higher rates of rectal STIs among lube users in one study¹³. However, this remains to be confirmed since we don't know which lubes were used by study participants, nor do we know if there is a cause-to-effect link in this study between the use of lube during AI and higher rates of rectal STIs.

One piece of the puzzle is the need to determine if lubes caused the rectal inflammation or cell damage observed in some studies. Other factors could have this effect. We need to consider the following:

- Some level of inflammation occurs naturally in the rectum, even among people without digestive or gastrointestinal problems.
- AI itself, as well as enemas and douching, causes some temporary damage.
- Most of that damage—if not all—repairs itself within minutes or hours after it occurs.

So we must be able to compare:

1. normal levels of inflammation and cell damage that occur naturally in the rectum,
2. levels of inflammation and damage that are a result of AI alone, without lubes, and
3. levels of inflammation and damage that are a result of AI with lubes.

[‡] Inflammation is one of our body's biological responses to something harmful, like a pathogen or a toxic product. On skin it can cause redness, increased heat, pain, and swelling that result from influx and activation of white blood cells. It is likely that this also occurs in a more subtle and asymptomatic way in the rectum where some activated white blood cells can also be a target for HIV infection.

Designing a study to assess these three different levels of inflammation and damage is critically important to better understand lube's effect—if any—on inflammation and damage.

Even if we were to discover that some lubes cause more inflammation and damage during AI compared to AI without lubes, we would still need to test whether this leads to a higher risk for acquiring HIV and STIs.



What does this mean? Should we—or shouldn't we—promote the use of lubes during AI?

Unfortunately, we have limited data that can be translated into useful information that the public can use to make choices about lubes at this time.

The use of male and female condoms is still considered the best way to reduce the risk of HIV and STI transmission during AI. In addition, use of condom-compatible lube has been associated with a decreased the risk of condoms breaking or slipping.¹⁴

For AI without a condom, it is not possible to recommend for or against using lubes at this time. Lube use on its own is not a proven method of HIV or STI prevention. It is unclear whether any particular lubes might increase, decrease or have no effect on acquiring HIV and other STIs. Therefore, it is not possible to make specific recommendations for or against specific brands of water-based or silicone-based lubes due to the limited research available at this time.

Clearly, we need to determine how to evaluate the safety of lubes for rectal use because we urgently need information that allows users to make better informed decisions about which products they use.

2: Is the question of lube safety similar to concerns about nonoxynol-9?

Nonoxynol-9 (N-9), the active ingredient found in most over-the-counter spermicides on the market today, was the first product to be tested as a potential vaginal microbicide.

Study results showed that N-9 can increase risk of acquiring HIV when used vaginally more than once a day.¹⁵ A separate study showed that even small doses of N-9 used rectally even one time can be highly damaging to rectal tissue in the period shortly after use. However, damage shown at 15 minutes after exposure to N-9 had completely healed by 2 hours.¹⁶ In another study of men using N-9 daily for up to 6 weeks, safety concerns were comparable between the N-9 and placebo groups.¹⁷

However, since potential exposure to HIV could happen relatively soon after a product with N-9 is applied rectally, perhaps this could increase risk of HIV infection through AI. However, no study has shown this.

Despite global efforts led by the Global Campaign for Microbicides to get N-9 removed from condoms and lubes (products that may be used rectally), a few brands still contain N-9.

While N-9 is still a viable option for contraception:

- **N-9 should not be used more than once a day vaginally.**
- **N-9 should never be used rectally.**



Don't regulators have to review safety data and approve lubes before they are available on the market?

IRMA is still looking into the level of regulatory oversight on lube safety. As we continue to consult with regulatory agencies in several countries (U.S., Canada, Peru, South Africa, UK) the following picture is emerging. *Please note that these are merely preliminary observations from IRMA, and are subject to changes and corrections as we learn more.*

- Regulators in various countries classify lubes in different ways, depending on the claims made by manufacturers. This results in the application of different sets of safety criteria for the exact same product in different countries. For example, the U.S. classifies lubes as medical devices, while Canada classifies them as cosmetics.
- The safety criteria for medical devices are usually stricter than the criteria for cosmetics. However, IRMA believes that the current criteria are probably insufficient based on the information we have from lube studies so far. The U.S. simply requires data from studies that test whether lubes irritate rabbit vaginas. Clearly, this is insufficient to tell us about their safety for rectal use in humans.
- In some contexts, some products sold as lubricants are on the market without having received any regulatory approval.
- Some regulatory agencies have little to no power or resources to force manufacturers to seek regulatory approval, or to take action regarding products that may not be safe.
- Even in jurisdictions where regulatory agencies have very clear and stringent safety criteria, and where they have the power and resources to enforce these rigorously, there may still be no requirement to demonstrate the safety of these products for rectal use, since manufacturers rarely indicate that their product is intended for that use.
- As an HIV and STI prevention field, we are still left with the problem of not having clarity around which rectal safety tests to recommend, even if regulatory bodies were willing to demand them of manufacturers. In this context, IRMA believes that regulators will hesitate to enforce tests that would only provide limited information about any demonstrably increased safety risks.
- IRMA urges caution when engaging with regulators. We know from the experience of reproductive health that pushing for stricter regulatory purview can lead to unintended consequences, like limiting important choices for consumers, when other actions might have been just as effective.

We will continue to monitor the situation and update our fact sheet accordingly.

IRMA calls for more research into the rectal safety of lubes.



How is IRMA advocating for more research on the safety of lubes used during AI?

The current paucity of data is a critical gap in knowledge and must be filled. Translating this type of data into useful information for users, funders, programme directors, and policy makers would be of significant benefit to the field. Lessons learned from this work will also provide valuable insights into product formulation, as well as message development on the safety and efficacy of vaginal and rectal microbicides, when these products become available.

To address this lack of information, IRMA launched a global web-based survey for 29 weeks in 2007 (An overview of the results from this survey can be found in IRMA's report: [Less Silence, More Science: Advocacy to Make Rectal Microbicides a Reality](#)). The survey provided extensive information on lube use, preferences, and acceptability among nearly 9,000 men, women and transgender people from over 100 countries, and established a prioritised list of the most widely-used lubes to test for rectal safety.¹⁸

In early 2009 IRMA convened a working group comprised of researchers and advocates to discuss the testing of sexual lubes for rectal safety. While the working group identified many scientific challenges that remain unaddressed to this day, there has been some progress.

IRMA's ongoing action on lube safety includes the following activities:

- Urging researchers to test lubes for rectal safety and to share their findings;
- Facilitating dialogue among leading researchers and advocates within the working group on rectal safety of lubes;
- Compiling articles and studies related to lube safety, particularly for rectal use, and maintaining an updated background document on this issue;
- Making IRMA's list of most widely-used lubes available to anyone interested in testing lubes;
- Monitoring how regulatory agencies in various countries address lube safety;
- Potentially engaging with lube manufacturers; and,
- Keeping IRMA membership updated on developments in this area.



What are rectal microbicides?

Currently in development, a rectal microbicide is a product that could be formulated as a gel with lube-like properties, a douche, or an enema used rectally to reduce a person's risk of HIV infection. Rectal microbicides could offer both primary protection in the absence of condoms and back-up protection if a condom breaks or slips off during AI.

For those unable or unwilling to use condoms, rectal microbicides could be a safe and effective alternative way of reducing risk, especially if they enhanced sexual pleasure and were unobtrusive enough to motivate consistent use.

Such alternatives are essential if we are to address the full spectrum of prevalent sexual practices and the basic human need for accessible, user-controlled HIV and STI prevention tools.

Vaginal microbicides are currently being developed as well. They should be tested to determine whether they are safe for rectal use, to ensure information is provided to users through appropriate product labelling and community education efforts.



Should we be worried about the safety of rectal microbicides as well?

IRMA is aware of the likelihood that some of the first rectal microbicides will be available in gels with lube-like properties. Therefore, avoiding confusing messages about lube safety now is paramount to avoid delays in access and use of an important public health tool later.

Researchers working on the development of rectal microbicides are very diligent about testing all candidate products. These are formulated in a way to ensure that they meet the strictest safety standards. They undergo a broad range of laboratory tests, including similar ones to those mentioned in relation to lubes in this fact

sheet, and many others. Only the products that appear to cause little to no cell damage, inflammation and toxicity move forward to the next stages of testing.

By late 2010, one rectal microbicide candidate—a product based on the antiretroviral drug UC781—had successfully completed a Phase I safety study among a small group of women and men, and no signs of safety concerns were found (An overview of the study can be found in Section 2.1.7 of IRMA’s report [From Promise to Product: Advancing Rectal Microbicide Research and Advocacy](#)). Two more candidate products based on the antiretroviral drug Tenofovir are in Phase I safety studies.

Each of these candidate products will only continue to be tested as potential rectal microbicides if they do well in human safety studies.



Who is IRMA?

International Rectal Microbicide Advocates (IRMA) is a global network of advocates, scientists, policy makers and funders from six continents working together to advance a robust rectal microbicide research and development agenda. Our goal: the development of safe, effective, acceptable and accessible rectal microbicides for the men, women, and transgender individuals who engage in anal intercourse and need options in addition to male and female condoms.

Get involved and learn more.

Visit IRMA’s [website](#). And click [here](#) for IRMA blog posts related to lubricants.

¹ Fuchs EJ, et al. “Hyperosmolar sexual lubricant causes epithelial damage in the distal colon: potential implication for HIV transmission”, *J Infect Dis*. 2007 Mar 1; 195(5): 703-10.

² Russo J, Dezzutti C, et al. “Safety and Anti-HIV Activity of Over-the-Counter Lubricant Gels,” Microbicides 2010 presentation (unpublished).

³ Sudol KM, Phillips DM. “Relative safety of sexual lubricants for rectal intercourse”, *Sex Transm Dis*. 2004 Jun; 31:346-9.

⁴ Sudol KM, Wallace R, Ford BE, Phillips DM. “Relative safety of OTC lubricants for rectal intercourse,” Microbicides 2006 poster (unpublished).

⁵ Begay O, et al. “Preliminary evaluation of toxicity and antiviral properties of personal lubricants,” Microbicides 2010 poster (unpublished)

⁶ Russo J, Dezzutti C, et al. “Safety and Anti-HIV Activity of Over-the-Counter Lubricant Gels,” Microbicides 2010 presentation (unpublished).

⁷ 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,” *J Biol Regul Homeost Agents*. 2004 Jul-Dec; 18(3-4): 268-74.

⁸ Baron S, Poast J, Nguyen D, Cloyd MW. “Practical prevention of vaginal and rectal transmission of HIV by adapting the oral defense: use of commercial lubricants,” *AIDS Res Hum Retroviruses*. 2001 Jul 20; 17(11): 997-1002.

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- ⁹ Gorbach PM, et al. "Rectal lubricant use and risk of rectal STIs," Microbicides 2010 presentation (unpublished).
- ¹⁰ Fuchs EJ, et al. "Hyperosmolar sexual lubricant causes epithelial damage in the distal colon: potential implication for HIV transmission", *J Infect Dis*. 2007 Mar 1; 195(5): 703-10.
- ¹¹ Russo J, Dezzutti C, et al. "Safety and Anti-HIV Activity of Over-the-Counter Lubricant Gels," Microbicides 2010 presentation (unpublished).
- ¹² Adriaens E, Remon JP. "Mucosal irritation potential of personal lubricants relates to product osmolality as detected by the slug mucosal irritation assay," *Sex Transm Dis*. 2008 May; 35(5): 512-6.
- ¹³ Gorbach PM, et al. "Rectal lubricant use and risk of rectal STIs," Microbicides 2010 presentation (unpublished).
- ¹⁴ Stone E, et al. "Correlates of condom failure in a sexually active cohort of men who have sex with men," *J Acquir Immune Defic Syndr Hum Retrovirol*. 1999 Apr 15; 20(5): 495-501.
- ¹⁵ Van Damme L, Ramjee G, Alary M, et al. "Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial," *Lancet*. 2002 Sep 28; 360(9338): 971-7.
- ¹⁶ Phillips DM, Taylor CL, Zacharopoulos VR, Maguire RA. "Nonoxynol-9 causes rapid exfoliation of sheets of rectal epithelium," *Contraception*. 2000 Sep; 62(3): 149-54.
- ¹⁷ Tabet S, Surawicz C, Horton S, et al. "Safety and toxicity of nonoxynol-9 gel for possible use as a rectal microbicide," *Sex Transm Dis*. 1999; 26: 564-571.
- ¹⁸ Javanbakht M, Murphy R, Gorbach PM, LeBlanc M, Pickett J. "Preference and Practices Relating to Lubricant Use During Anal Intercourse: Implications for Rectal Microbicides," *Sexual Health*. 2010 Jun; 7(2): 193-8.

