*Advances in Contraception* 7 (1991) 291–300




# The CU SAFE 300 IUD, a new concept in intrauterine contraception: first-year results of a large study with follow-up of 1017 acceptors

K.H. KURZ AND P.A. MEIER-OEHLKE

*Department of Obstetrics and Gynecology, IRIR – International Research Institute for Reproduction, Kaiser-Wilhelm-Ring 22, 4000 Düsseldorf II, Germany*

**Abstract**

After more than a decade of basic research with the help of cavimetry, retentiometry, X-ray and ultrasonography, a new intrauterine contraceptive device, the CU SAFE IUD, was developed. The plastic body of the device shows the following properties: uterine cavity compatible, enhanced flexibility, low surface area, fundus-seeking anti-expulsive design, no anchoring mechanisms, and one monofilament without a knot embedded into the shaft. The copper surface area of 300 $mm^2$ guarantees a high efficacy for up to five years. The CU SAFE 300 IUD fulfils all requirements of the International Organization for Standardization (ISO) in regard to intrauterine devices.

This paper reports on the first-year results of a large ongoing CU SAFE 300 study, number of insertions 1150. 1017 acceptors of all fertile age groups accumulated 10,576 woman-months of use. The event rates were as following: pregnancy 0.6; expulsion 0.6; removal for bleeding 4.2, for pain 1.5; infection 0.0; other medical 0.9; non-medical 3.1. The continuation rate was 89.1 at the end of the first year.

The increased safety and high efficacy of the CU SAFE 300 provides comfort for both user and partner. The ease of insertion without a plunger and gloves (inserter tube diameter 3 mm) and the ease of removal (force of traction ~1 N) mean safety also for the medical and paramedical fitter of the CU SAFE 300 IUD.

This paper is based on a presentation given at the Seventh International Meeting of the Society for the Advancement of Contraception, which was held in Singapore on 4–11 November, 1990.

## Introduction

Before 1970, mainly plastic IUD models were used with relatively high pregnancy rates between 3.0 to 6.0. To reach failure rates below 10.0, plastic IUDs need a large surface area that distends the average uterine cavity. However, these IUD properties increase the expulsion rates, through intensified contractions of the uterus, and the removal rates for bleeding and pain.

More efficacy was reached in the decade 1970–1979 witnessing a proliferation of new, mainly copper medicated IUDs. The copper IUDs tend to have lower expulsion rates than the non-medicated IUDs, reflecting design improvements in either the devices or the inserters, or both. The plastic bodies of the several models of copper IUDs are smaller.

In spite of the improvements, of which the most important one being the increase of efficacy, a lack of safety still exists with modern copper IUDs. Relatively high rates of removal for medical reasons, like bleeding and pain, and of expulsion remain the unfavorable outcome.

Furthermore, complicated insertion techniques still contribute to reduced use of IUDs, as does, for example, the breaking-off of the control threads or a plastic arm, because of excessive holding strength during removal of certain IUD models. In this context, it should be mentioned that a substantial number of IUD users suffer from unwanted side-effects, but do not terminate intrauterine contraception because of the incompatibility of other contraceptive methods or because they object to other methods on personal grounds.

## Materials and methods

Extensive *in vivo* basic research was carried out on a great number of fertile women of all ages and parities [1,2]. Cavimetry (determination of uterine cavity length and width), retentiometry, X-ray and ultrasound were used to create an IUD with the following clinical properties: ease of insertion and removal, high efficacy, improved safety, and low expulsion rates.

The device, named CU SAFE 300, consists of a T-shaped plastic body (Figure 1). The ends of the flexible transverse arms are inwardly bent, providing a non-irritating, fundus-seeking mechanism. Only one monofilament without a knot is integrated in the IUD shaft. A wire of copper, purity 99.99%, with a total surface of approximately 300 $mm^2$, is wound tightly on the vertical stem of the device (Figures 2 and 3). Models of CU SAFE medicated with copper of 250 $mm^2$ and 200 $mm^2$ have shown comparatively good results in ongoing clinical trials.

Summary of the CU SAFE IUD's properties:

a) Uterine cavity adapted design
b) Low surface area
c) Fundus seeking mechanism
d) High flexibility
e) No anchoring protrusions
f) Monofilament integrated in the shaft without a knot
g) Thin inserter tube (diameter 3 mm) without a plunger.

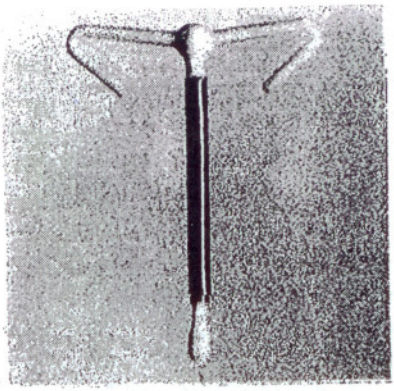

Figure 1 Design of the CU SAFE 300 IUD

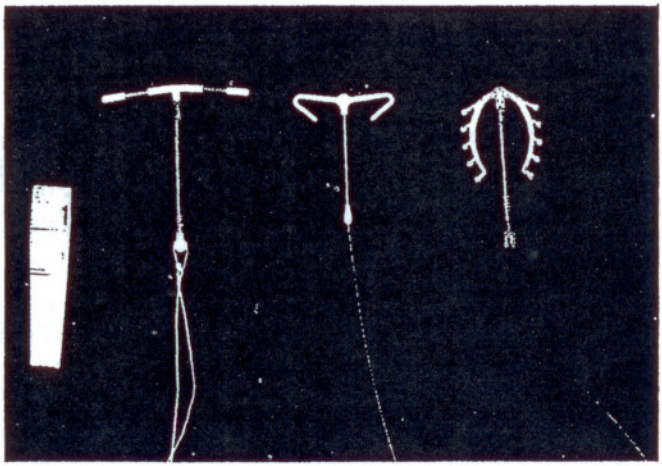

Figure 2 For comparison: the CU SAFE 300 IUD between the T Cu 300 (left) and the Multiload 250

The objectives of this study are to determine the efficacy, safety, rates of expulsion, and continuation rates of the CU SAFE 300 IUD in a large interval insertion trial.

The investigators decided to conduct an open non-comparative trial for the following reasons:

a. A previous large study, using the CU SAFE 250, number of insertions 714, had already shown remarkable results at the end of the first year: pregnancy rate 0.6, expulsion rate 0.8, removal rates for bleeding 2.7, and for pain 0.6.

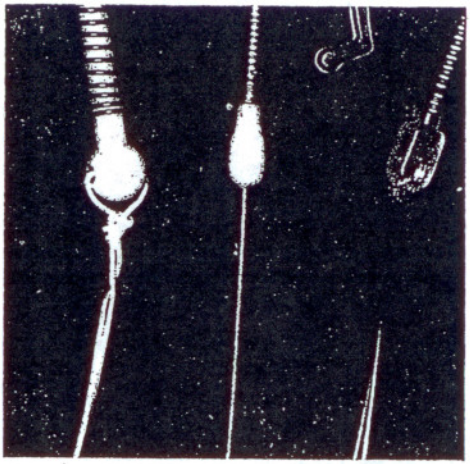

Figure 3 Thread-shaft connections of several IUDs. From left to right: T Cu IUD, CU SAFE IUD, Multiload

b. Some of the disadvantages of currently distributed IUD-models are: two control threads with a knot; complicated insertion procedure if a plunger is used (risk of perforation); complicated removal if strong holding forces of more than 10 N are to be overcome with the risk of breakage of one arm; lack of radiopacity and most important, oversize of the plastic body and its consequences [3–5].

c. A randomized comparative trial testing the CU SAFE 300 against approximately 20-year-old models of copper IUDs would provide unnecessary risks for the health of 50% of the participants. In addition, a number of women interested in IUD use for contraception previously refused to accept the usual copper IUD models and generally chose the CU SAFE IUD for themselves.

Under these circumstances, a comparative trial was considered to be unethical.

The CU SAFE 300 was inserted in 1150 women of all age and parity groups between January 1987 and July 1989. All acceptors were currently exposed to the risk of pregnancy, in good general health with normal menstrual cycles and showed neither contraindications nor other criteria of exclusion.

Age and parity groups are demonstrated in Figure 4. The majority of the women in this cohort were nulliparous. However, at the time of acceptance only 27% of the acceptors were less than 25 years of age. The IUDs were inserted mainly at the end of menstruation or within the subsequent two days.

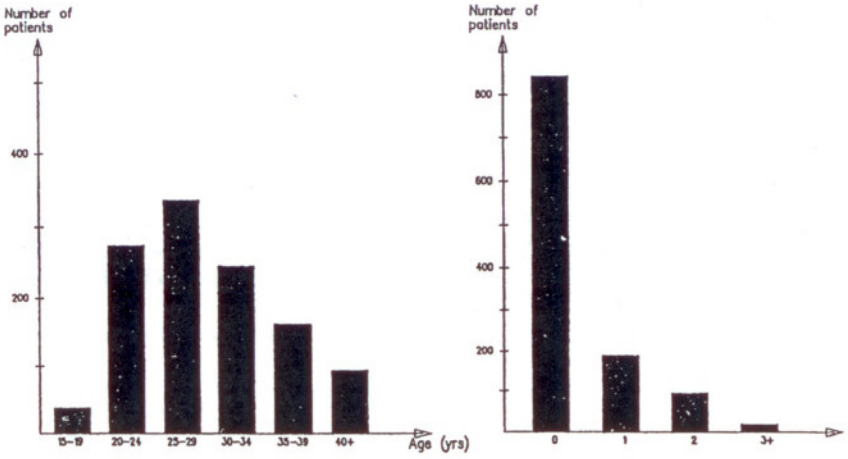


**Figure 4** *(left)* Distribution of age; *(right)* Distribution of parity

## Results

Adequate follow-up could be obtained in 1017 acceptors. One hundred and thirty three of the users were lost to follow-up, the majority due to a change of residence. By the end of the first year 10,576 woman-months of use had been accumulated (Table 1).

### *Pregnancy rates*

A total of 5 pregnancies were recorded for a cumulated pregnancy rate of 0.6 per 100 (Table 1). None of the pregnancies were ectopic and in any case the CU SAFE 300 was located either intrauterine or partly intracervically as confirmed by ultrasound.

### *Expulsion rates*

Five expulsions occurred, a cumulation rate of 0.6 per 100.

### *Removals for bleeding*

Removals for this reason constituted the major single category of termination. The number of events was 37 and the rate was 4.2 per 100 at the end of the year. There was an approximately even accumulation over the year, as can be seen on the graph, unlike all other medical events (Figure 5).

*Removals for pain*

CU SAFE 300 IUDs had to be removed 13 times for this reason, resulting in a rate of 1.5 per 100.

*Other medical removals*

During the observation time, there were 8 medical removals. The main causes were continuous vaginal discharge or adnexal cysts scheduled to be ectomized combined with an abrasio. Remarkably, no infection, confirmed by bimanual investigation, purulent cervical discharge, and laboratory tests, was diagnosed.

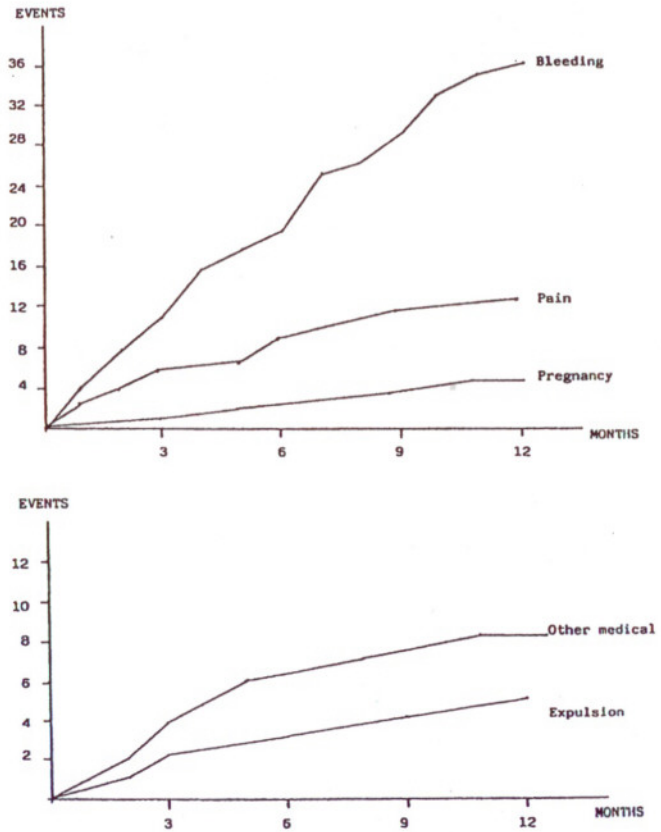


**Figure 5** Graphical demonstration of cumulative events during use of CU SAFE 300

*Non-medical removals*

The number of these events, mainly the desire to become pregnant or no further need of contraception, cumulated to 27 over the year, the rate being 3.1 per 100.

*Continuation rate*

The continuation rate at the end of the first year was 89.1, with a total number of events of 95 (Table 1).

**Table 1 First-year cumulative rates per 100 acceptors of the CU SAFE 300 and the cumulative number of events**

| | *Rates* | *Events* |
|---|---|---|
| Pregnancy | 0.6 | 5 |
| Expulsion | 0.6 | 5 |
| Medical removal | | |
| bleeding | 4.2 | 37 |
| pain | 1.5 | 13 |
| infection | – | – |
| other medical | 0.9 | 8 |
| Non-medical removal | 3.1 | 27 |
| Continuation | 89.1 | |

Number of followed-up acceptors: 1017
Controlled woman-months of use: 10,576

## Discussion

The present study is one of several ongoing, partly multicenter and comparative trials. Like in another study [6], the CU SAFE 300 manifested a high degree of effectiveness, with a failure rate of 0.6 in a cohort of 1017 acceptors cumulating 10,576 controlled woman-months of use at the end of the first year. This is particularly remarkable, since more than the half of the CU SAFE 300 (56.3%) users were less than 30 years old, the age of highest fecundity. Previous studies [7,8] showed that age differentials markedly affect pregnancy rates with copper IUDs, the rates declining as age increases. The present study confirms these findings. Four of the five pregnancies occurred in the age group 20–24 years. Additional measures, such as the use of barriers during the time of peri-ovulation, may further reduce the pregnancy rates with IUDs.

The high efficacy of the CU SAFE 300 corresponds with that of other models having a relatively large surface area of copper: 380 $mm^2$ [9] and 375 $mm^2$ [10].

Table 2 shows the results of this study and compares them with the first-year results of a study testing the TCu380 inserted and followed up in 1051 acceptors [9]. Nulliparity in the present CU SAFE 300 study was 73.5%. In the TCu380 study, conducted by the Population Council, 80.8% of the acceptors were nulliparous. At the end of the first year, the pregnancy rate of the CU SAFE 300 was 0.6, compared with the respective pregnancy rate of 0.9 found in the TCu380 study.

Although the CU SAFE 300 IUD's relatively small copper surface area of 300 $mm^2$, 79% of the 380 $mm^2$ of TCu380, the somewhat lower pregnancy rate of the former IUD may be due to its extremely low expulsion rate of 0.3. In comparison, the expulsion rate of the TCu380 was 5.8. It has been suggested that about 30% of IUD failures occur because of unmentioned expulsion [11].

**Table 2 CU SAFE 300 and TCu380 IUDs: cumulative event rates per 100 users of the present and an earlier study [9] at the end of the first year**

| | *CU SAFE 300* | *TCu380A* |
|---|---|---|
| Number of acceptors | 1017 | 1051 |
| Controlled woman-months of use | 10576 | 9804 |
| Pregnancy | 0.6 | 0.9 |
| Expulsion | 0.6 | 5.8 |
| Removals | | |
| bleeding/pain | 5.7 | 11.1 |
| infection | 0.0 | not categorized |
| other medical | 0.9 | 3.5 |
| non-medical | 3.1 | 3.0 |
| Continuation rate | 89.1 | 75.7 |

Age and parity groups in both studies are comparable

The removal rate of 4.2 for bleeding constituted the major single category of termination. Removals for pain were approximately one third (rate 1.5) compared to the removals for bleeding. It should be mentioned that, in most cases of removal for continuous bleeding, spotting, and heavy menstruation, pain was minor or no problem. The reduction of pain reflects a major increase in safety, acceptance, and recommendation to potential users of the CU SAFE 300 IUD.

Applying the usual investigational methods, including laboratory tests, no case of infection of the upper female genital tract could be detected in the 1017 CU SAFE 300 acceptors. In all cases of removal for bleeding and/or pain, endometrial tissue was examined by a pathologist. In no case were signs of endometritis found. It is suggested that the rates of PID (infection of the upper female genital tract) are overestimated in users of copper IUDs compared with non-users of contraception. *In vitro* investigations proved that new and used copper has not only spermicidal [12] but also antibacterial and antichlamydial properties [13,14]. The oligodynamic,

bacteriostatic and bactericidal properties of metals like copper and zinc have been known and used for therapeutic purposes by physicians for many centuries.

No perforation with a CU SAFE 300 occurred. The correct intrauterine position of the CU SAFE 300 was confirmed immediately after each insertion by ultrasound. Perforation is reported to occur nearly exclusively with insertion procedures using a plunger [3]. The CU SAFE 300 uses a flexible inserter tube with a diameter of only 3 mm. The crossbar of the IUD being unfolded at the tip of the inserter additionally reduces penetration and perforation of the uterine muscle.

The cervical canal had to be dilated after the application of a paracervical block in 12 cases. The 95 removals were free of complications and the copper wire of all devices was free of breakage.

## Conclusion

The CU SAFE 300 IUD is the first classical copper IUD which was developed by basic research using cavimetry, retentiometry, X-ray and ultrasound. The data obtained were mainly used to invent a new IUD plastic body which helped to fulfill all IUD requirements of the International Organization for Standardization (ISO) [4], among them 'ease of insertion and removal' and 'radioopacity of all parts of the IUD'.

The first-year results of this large ongoing study prove that advances in intrauterine contraception, particularly with regard to safety, are possible without loss of efficacy. The use of a plunger-free insertion procedure further reduces perforation. This increase in safety and the ease of insertion and removal is of special importance for medical and trained paramedical personnel.

It is hoped that the CU SAFE IUDs may also be inserted and removed by village midwives in third world countries, making effective and safe, long-acting, reversible contraception for child spacing increasingly available in rural areas.

## References

1. Kurz, K.H., Tadesse, H. and Haspels, A.A. (1984). In vivo measurements of uterine cavities in 795 women of fertile age. *Contraception*, 28, 495
2. Kurz, K.H. (1982). IUD technology. Role of retention in avoiding expulsion of IUDs – measuring devices for basic research. *Contracept. Deliv. Syst.*, 3, 107
3. WHO Scientific Group (1987). Mechanism of action, safety and efficacy of intrauterine devices: *World Health Organization, Technical Report Series 753*, pp. 46–48
4. ISO, International Organization for Standardization (1981). Mechanical contraceptives – intrauterine devices. *Technical Report* 7493
5. Kurz, K.H. (1985). Cavimeter uterine measurements and IUD clinical correlation. In: Zatuchni, G.I., Goldsmith, A. and Sciarra, J.J. (eds.) *Intrauterine Contraception: Advances and Future Prospects*. Harper and Row, Philadelphia, p. 142
6. Thiery, M. *et al.* (1991). Personal communication on unpublished data
7. Jain, A.K. (1975). Safety and effectiveness of intrauterine devices. *Contraception*, 11, 243
8. Sivin, I. and Stern, J. (1979). Long acting, more effective copper IUDs: a summary of US experience, 1970–1975. *Stud. Fam. Plann.*, 10, 263
9. Sivin, I. and Tatum, H.J. (1981). Four years of experience with the TCu380: a intrauterine contraceptive device. *Fertil. Steril.*, 36, 159

10. Thiery, M., van der Pas, H. and van Kets, H. (1985). The ML Cu 375 intrauterine contraceptive device. *Adv. Contracept.*, 1, 37
11. Mishell, D.R. Jr (1975). Assessing the intrauterine device. *Fam. Plann. Perspect.*, 7, 103
12. Alvarez, F., Brache, V., Fernandez, E., Guerrero, B., Guiloff, E., Hess, R., Salvatierra, A.M. and Zacharias, S. (1988). New insights on the mode of action of intrauterine contraceptive devices in women. *Fertil. Steril.*, 49, 768
13. Mandouvalos, H. and Gouskos, A. (1981). Germicidal effect of pure electrolytic copper on the gonococcus. *Contracept. Deliv. Syst.*, 2, 225
14. Kleinman, D., Sarov, I. and Insler, V. (1989). Inhibition of chlamydia trachomatis growth in endometrial cells by copper: possible relevance for the use of the copper IUD. *Contraception*, 39, 665

**Resumé**

Après plus d'une dixaine d'années de recherche fondamentale s'appuyant sur la cavimétrie, la rétentiométrie, la radiographie et l'ultrasonographie, un nouveau DIU a été mis au point. Il s'agit du DIU CU SAFE, dont le corps en plastique présente les propriétés suivantes: compatibilité avec la cavité utérine; plus grande souplesse; faible superficie; de conception l'amènant à se placer au fond de la cavité et empêchant l'expulsion; aucun mécanisme d'ancrage; un seul filament sans nodosité enfoncée dans la cavité. La surface recouverte de cuivre sur 300 $mm^2$ garantit une efficacité importante pour plus de 5 ans. Le DIU CU SAFE 300 est conforme aux normes de l'ISO (Organisation internationale de normalisation) pour les dispositifs intra-utérins.

Cet article rend compte des résultats de la première année d'une étude en cours sur le CU SAFE 300, le nombre d'insertions ayant été de 1150. Ce dispositif a été posé chez 1017 femmes de tous les groupes d'âge en période de fertilité, représentant un total de 10,576 mois-femme d'utilisation. Les pourcentages des événements survenus sont: grossesses 0.6; expulsions 0.6; retraits pour hémorragie 4.2; pour douleurs 1.5; infections 0.0; autres problèmes médicaux 0.9; non médicaux 3.1. Le taux de poursuite était de 89.1 à la fin de l'année.

La sécurité accrue et la haute efficacité du CU SAFE 300 proviennent du manque d'inconfort à la fois pour la femme et pour son partenaire. La facilité de son insertion, partiquée sans poussoir ni gants (tube à insertion d'un diamètre de 3 mm), et de son retrait (force de traction ~ 1 Newton) apportent aussi une sécurité pour le technicien médical et paramédical lors de la pose et du retrait du dispositif.

**Resumen**

Después de más de un decenio de investigaciones básicas con la ayuda de cavimetría, retenciometría, radiografía y ultrasonografía, se desarrolló un nuevo DIU. Se trata del DIU CU SAFE, cuyo cuerpo de plástico tiene las siguientes propiedades: compatibilidad con la cavidad uterina; mayor flexibilidad; superficie pequeña; tendiente a buscar el fondo e impedir la expulsión; ningún mecanismo de anclaje; un solo filamento sin nudo adentrado en la cavidad. La superficie recubierta de cobre de 300 $mm^2$ garantiza un alto nivel de eficacia por un período hasta de 5 años. El DIU CU SAFE 300 satisface todas las normas de la ISO (Organización Internacional de Normalización) relativas a dispositivos intrauterinos.

Esta monografía informa sobre los resultados del primer año de amplio estudio que se realiza con el CU SAFE 300, con un número de inserciones que ascendió a 1,150. Este dispositivo fue colocado en 1,017 mujeres de todos los grupos de edad fecunda, que representaron en total 10,576 meses-mujer de utilización. Los porcentajes de acontecimientos ocurridos son: embarazos 0.6; expulsiones 0.6; retiros por pérdidas de sangre 4.2; por dolores 1.5; infecciones 0.0; otros motivos médicos 0.9; no médicos 3.1. La proporción de continuación fue de 89.1 al finalizar el primer año.

La seguridad aumentada y la major eficacia del CU SAFE 300 proporciona confort tanto a la mujer como a su compañero. Su facilidad de inserción, practicada sin émbolo ni guantes (el tubo de inserción tiene 3 mm de diámetro) y de retiro (fuerza de tracción ~ 1 Newton) también brinda seguridad al técnico médico o paramédico al colocar o retirar el DIU CU SAFE 300.