Vaginal Rejuvenation Post Market Review
Summary of Devices Clinical Section Device Assessments s 47E(d) and s 47F

s 47E(d) and s 47F
[redacted]
[redacted]

Gaudeamus igitur, iuvenes dum sumus

- While the subject matter under examination may, in human terms, be highly ranked in terms of interest and importance, this presentation is of necessity somewhat vague, unscientific and inexact in keeping with calibre of literature available and the description of the particular field of interest being vague, unscientific and inexact.

Rejuvenation

- To make young or youthful again: give new vigour or to restore to an original or new state.
- Refresh, renew, renovate and restore. While all these words mean ‘to make like new,’ rejuvenate suggests the restoration of youthful vigour, powers, or appearance.
- **Advert [USA]**: **Is Financing Available for Vaginal Rejuvenation?**
- Yes! If your insurance does not cover your vaginal tightening procedure, we have a variety of easy and convenient 3rd party financing options. CLICK HERE to learn more.

- Complaints of chronic vulval and vaginal discomfort, irritation, dryness, itching, pain and inability to tolerate sexual intercourse are widespread.
- The topic is one of the most personal and intimate subjects for which a woman may find herself having to seek medical assistance.
- Some of the saddest cases we see involve relationship break-up.
- There must be an unshakeable trust between the woman and her doctor, male or female.
- In the best of faith, the quest for a solution to these problems can be fraught with difficulty and commonly there is incomplete resolution.
- Desperate women, whose relationships are in trouble, may be willing to try very costly, fringe treatments, encouraged by slick advertising.

Putative indications for treatment

- Vaginal rejuvenation indications include: vaginal dryness, dyspareunia, itching and burning sensations, vulvo-vaginal irritations, recurring vaginitis and cystitis, mild stress urinary incontinence (SUI), reduced sensitivity and vulvar ageing, genito-urinary syndrome of menopause (GSM), vulvo-vaginal laxity, vulvar rejuvenation, and pelvic organ prolapse and improving sexual function
- Management/repair of female genital mutilation

Why would someone seek vaginal rejuvenation?

- The majority of women who present, seek vaginal rejuvenation for cosmetic reasons. As with any cosmetic surgery it is important for the patient to consider why they want the surgery before moving forward with it. Improving self-confidence usually plays a large part in the decision.
- It's important that the patient is inquiring about these procedures for herself, and not because of the wishes of a partner or pressure from society.
- It's also important that women looking into vaginal rejuvenation have realistic expectations of the outcomes. No cosmetic procedure is going to restore any part of the body to the way it was in youth. Importantly the vagina has wide variety of "normal anatomy."

Some context

- There are thousands of products and procedures marketing to women which claim to help them hold on to youth as long as they can. Vaginal rejuvenation falls into that category with promises of tightening the vagina, stopping incontinence, eliminating vaginal dryness, and more.
- There is potentially a massive market for something which really works
- There is potentially a massive market for something which can be sold as claiming to work but which may not.

• INTERNET ADVERTS

- Non-invasive, non-surgical vaginal rejuvenation is an amazing new technology that helps eliminate urinary leaks and improves vaginal health, tightness and sexual sensation. But with a few different technologies available on the market – marketed under different brand names – how does a women know which treatment is best for her?
- Dr. *** [USA] has already helped hundreds of women in the *** area stop bladder leaks & improve sexual intimacy with just a single 30 minute vaginal rejuvenation treatment. In this article he explains the differences between the two primary vaginal tightening technologies.
- Vaginal rejuvenation consists of surgical and nonsurgical treatments that firm up the skin around your vagina or tighten the vaginal canal. It helps improve issues such as sexual dysfunction, urinary incontinence and vaginal dryness.

- Energy-based devices deliver pulsated energy targeted to treatment areas. The majority of the laser devices have multiple indications including dermatological application; whilst some devices are intended solely for gynaecological purposes. Often these kinds of devices come with an applicator/handpiece intended to be used for vaginal rejuvenation.
- The term ‘vaginal rejuvenation’ encompasses a range of aesthetic and functional procedures that claim to correct and restore the optimal structure of the vagina and surrounding tissues.
- These devices harness laser (mostly $CO_{2,}$) or radiofrequency (RF) waves to heat the connective tissue of the vaginal wall to approximately 40°C to 42°C, aiming to induce collagen contraction, neocollagenesis, vascularization, and growth factor infiltration.
- The aim is to revitalize and restore the elasticity and moisture of the vaginal mucosa by stimulating blood circulation and collagen regeneration to strengthen the vaginal lining. The lasers are promoted as inducing controlled thermal injury to the epithelial layer of the vaginal skin, which then stimulates tissue repair and remodelling through the process of wound healing. It has been suggested that this process induces fibroblasts to produce collagen.

- Volva,-ae (s.f.I), or vulva,-ae = genitalia feminina externa, female external genital organs
- The vagina is the muscular canal that connects all that external genitalia to the uterus.

- The word vagina is often misused, notably in the lay press, to describe the vulva — which correctly refers to the external genitalia but not the *internal* structures in the area.

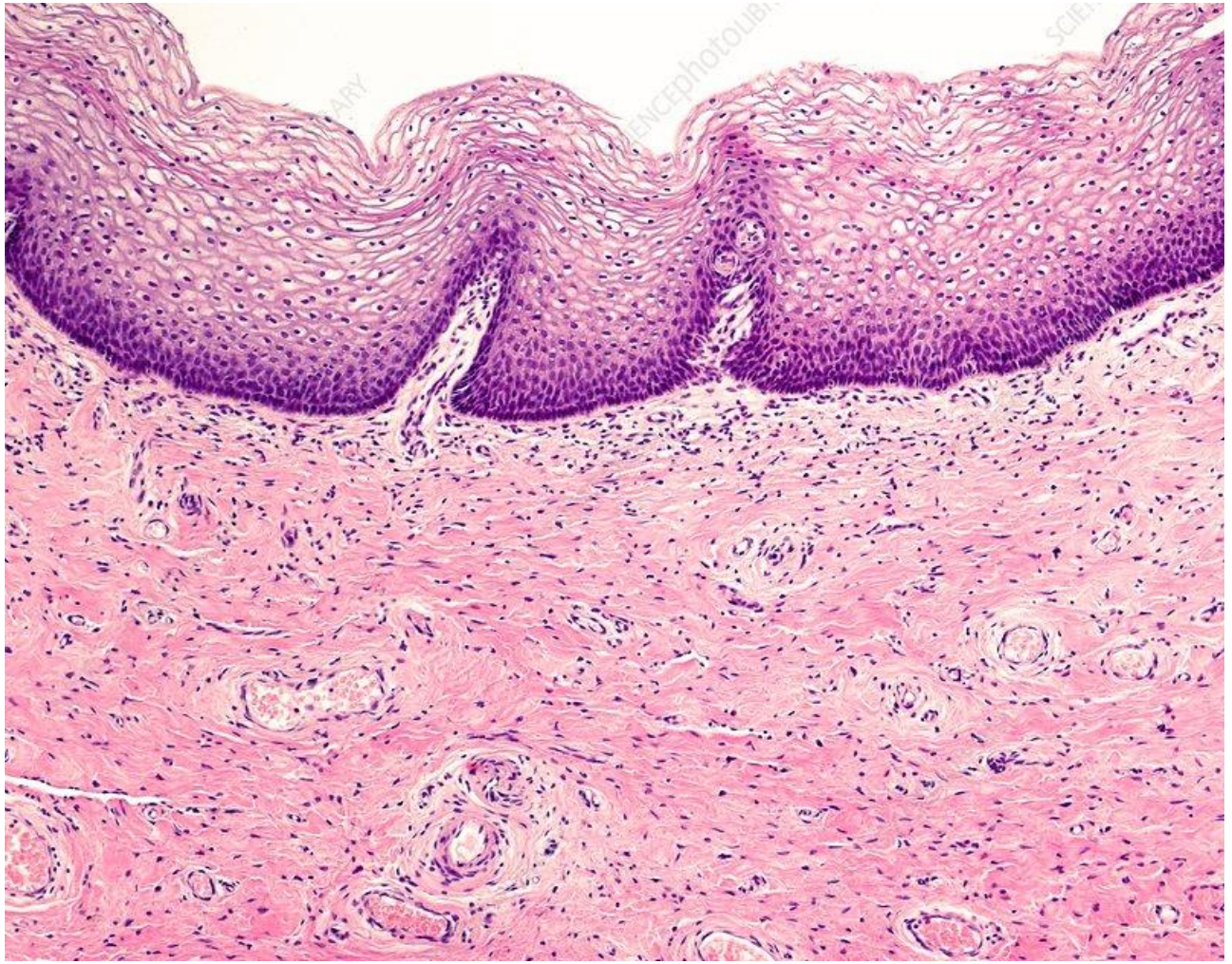
- **Keratinized Epithelium**
- The stratum corneum is the outermost layer that is composed of keratinized squamous cells. These keratinized cells are actually dead cells that shred periodically. They form an effective barrier against abrasions.
- Here, the protoplasm of the cell is replaced by a protein called keratin. This protein layer is usually dry and is impermeable to water. Thus, it acts as a better protective layer.
- **Nonkeratinized Epithelium**
- The stratified squamous epithelial cells that lack the keratin are called the nonkeratinized epithelium. It is found in various sites around the body including the vagina. This nonkeratinized epithelium is mostly moist and acts as a less effective barrier.
- Depending on age and damage, certain nonkeratinized surfaces also show a minor layer of superficial keratin.

- The vulva has both keratinized and nonkeratinized epithelium. On the labia majora, mons pubis and perineal region, the epithelium is keratinized and is similar to skin at other body sites.
- The epithelium that covers the hymen, vestibule and inner surfaces of the labia minora is a nonkeratinized, mucosal type.
- The vagina is lined by **non-keratinized** stratified squamous epithelium.

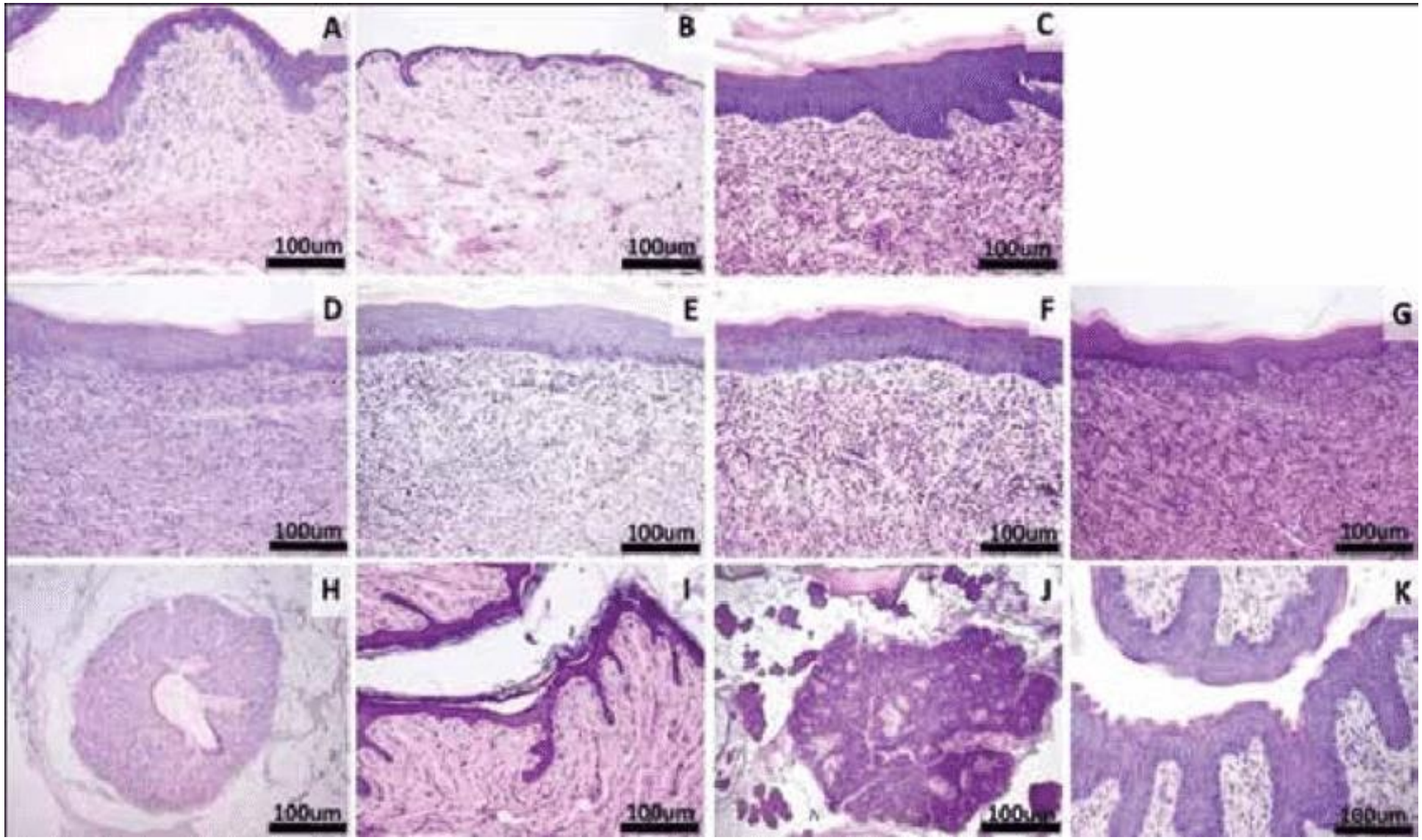
The effect of oestrogen on pre-pubertal and post menopausal vaginal epithelium

- In young girls before puberty, in lactating women and in the post-menopause, the vaginal epithelium is **thin and comprised of only basal and parabasal layers**. With exposure to oestrogen in the reproductive years, the vaginal epithelium thickens and develops a distinct cornified layer. Post-menopausal oestrogen replacement has a similar effect.
- The vaginal epithelial cells accumulate glycogen as they approach the surface. With H&E or trichrome stain, these glycogen-loaded cells appear "empty," with unstained cytoplasmic spaces.

Light micrograph oestrogenised human vagina



- After menopause the vaginal epithelium thins, glycogen stores diminish and the stratum corneum shows *variable degrees of keratinization*.
- Effects of oestrogenic replacement therapy on vaginal (A, B, C, D, E, F, G). Control group (A) showing normal histology; ME group, vaginal epithelial atrophy (B); Oestrogen replacement therapy submitted animals exhibited marked epithelial hyperplasia, characterised by an increased number of cellular layers and thickness


A
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The regular management of atrophic vaginitis

- There is little argument that the application of oestrogen to the atrophic vaginal epithelium is the gold standard for the management of the constellation of symptoms which accompany oestrogen lack.
- The application of oestrogen may be by some sort of systemic approach or by local application.
- This is a vast subject which cannot be adequately expanded upon here but the basic truth is well established.
- In pure, uncomplicated vaginal atrophy, the application of local oestrogen begins to work in a few days and is generally greatly appreciated.

Contraindications to oestrogen replacement therapy

- Breast cancer – actual
- Breast cancer – risk
- (Treated Endometrial cancer)
- (Thrombophilia)
- (Active liver disease)

Application of heat to skin

- Skin permeability has been shown to be a very strong function of temperature and less so of duration.
- Laser treatment of the skin has been shown to increase skin permeability.
- Energy sources such as Radio Frequency, CO2 or Erbium YAG LASERs may be used to apply heat to vaginal skin.

Radio frequency (RF) energy device

- RF applied to the vaginal wall has been shown to stimulate proliferation of glycogen-enriched epithelium, neovascularization, and collagen formation by creating heat via impedance, as an electric current is conducted through the target tissues. Once these devices generate temperatures between 40°C and 45°C, an inflammatory cascade is initiated and heat shock proteins induce fibroblasts, which leads to neocollagenesis and elastogenesis. By controlling temperature at this level, new cells generate rather than forming scar tissue.
- Example (Australian): 90 – 240Vac 50/60Hz – 150 VA, 1 MHz dynamic quadripolar, 25W adjustable 5 – 100%

Erbium YAG (Yttrium, Aluminium, Garnett) LASER

- An *Er*:*YAG laser* (*erbium*-doped yttrium aluminium garnet laser, *erbium YAG laser*) is a solid-state laser whose active laser medium is *erbium*-doped yttrium. It produces laser irradiation in the near infrared portion of the electromagnetic spectrum.
- Typical settings for erbium YAG laser employed for birthmarks, age spots and superficial skin ablation are wavelength 2940 nm, short pulse, laser output **2.5–5 J/cm^2**, and pulse duration 250 microseconds.
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Neodynium: YAG LASER

- **Nd:YAG** (**neodymium-doped yttrium aluminum garnet**; **Nd:$Y_3Al_5O_{12}$**) is a crystal that is used as a lasing medium for solid-state lasers. The dopant, triply ionized neodymium, Nd(III), typically replaces a small fraction (1%) of the yttrium ions in the host crystal structure of the yttrium aluminum garnet (YAG), since the two ions are of similar size. It is the neodymium ion which provides the lasing activity in the crystal. Nd:YAG lasers are optically pumped using a flashtube or laser diodes. These are one of the most common types of laser and are used for many different applications. Nd:YAG lasers typically emit light with a wavelength of 1064 nm, in the infrared.

Er:YAG or CO2

- Both the CO_2 laser and the EnYAG laser achieve tissue ablation through their affinity for **water**. However, the Er:YAG, which emits a wavelength of 2940 nm, has an affinity for water greater than 10 times that of the CO_2 laser, which emits a wavelength of 10,600 nm. The absorption characteristics of the laser determine the depth of penetration and the thermal dispersion. Energy that exceeds the thermal containment time of water is dispersed to the surrounding tissue as heat for remodeling. The high affinity of the Er:YAG for water coupled with a shortened pulse time enables the laser energy to be more completely absorbed in *cellular ablation* and therefore produces *minimal collateral thermal effect.* This is in contradistinction to the CO_2 laser, which has greater penetration, as well as *greater thermal dispersion.*
- The ablation (energy) threshold of the Er:YAG is accepted to be 0.5 through 1.6 J/cm^2, whereas that of the CO_2 is 5 J/cm^2.1 However, the tissue response is a complex interaction of wavelength, power, spot size, beam profile (Gaussian vs Top Hat), and duration. Wavelength and absorption alone are only part of the reason for the shallow penetration of the Er:YAG laser; the shortened pulse time must also be considered.

- The depth of penetration of the Er:YAG is 10 to 30 μm, and the adjacent thermal scatter is less than 5 μm; the depth of penetration of the CO_2 is 100 to 120 μm, with thermal scatter of 50 to 60 μm. Therefore to achieve the same depth, the Er:YAG requires more passes but allows for greater control with each pass. In general, the CO_2 laser removes the epidermis in the first pass, but the Er:YAG requires two to three passes to penetrate into the upper papillary dermis. The absence of significant *collateral* thermal damage means that the multiple ablative passes used with the Er:YAG laser are potentially less likely to lead to scarring. This contrasts with the thermal damage and scarring known to occur occasionally at a similar depth with the pulsed CO_2 laser.
- One of the key effects of the CO_2 laser is the heating of dermal collagen and subsequent collagen shrinkage during reformation. Unfortunately this thermal effect has also been blamed for the scarring occasionally seen with the CO_2 laser. Because of its absorption characteristics and shortened pulse time, the Er:YAG laser has almost no remodeling thermal effect. However, it may also lack the collagen shrinkage effect presumed to be present with CO_2 lasers.2 The thermal effect, however, does not *seem to be critical* to the efficacy of the treatment and the Er:YAG has proven almost as effective as the CO_2 laser.
- Thus: although **Erbium:YAG lasers do not penetrate as deeply as CO2 lasers**, they're able to mimic the effects of CO2 lasers by multiple passes, stacking and increasing the pulse duration while limiting the risk of unwanted side effects

- Subjects treated with Er:YAG laser recover more quickly from the procedure than those receiving CO_2 laser treament.
- The use of high-energy pulsed and scanning carbon dioxide (CO_2) lasers (10,600 nm) typically restrict the laser-tissue interaction time to less than 1 millisecond (thermal relaxation time of the upper part of the skin interacting with the laser) so that thermal diffusion is limited during the laser pulse. The resulting band of residual thermally altered collagen normally measures less than about 150 µm.[1] One of the limitations of CO_2 laser is the incidence of adverse effects, specifically prolonged erythema and dyschromias. The degree of postoperative erythema and time for re-epithelialization keeps most subjects at home for about 2 weeks.
- The erbium:YAG (Er:YAG) laser (2940 nm) represents an opportunity to decrease the thermal damage observed with the CO_2 laser. This wavelength is strongly absorbed by water (absorption coefficient 12,000 vs 800 cm^{-1} for CO_2) so that residual thermal damage has been shown to be less than about 50 µm vs the 80 to 150 µm typically observed after multiple passes of pulsed CO_2 laser exposure. Also, it has been shown that Er:YAG laser wounds re-epithelialize earlier than CO_2 laser wounds.[2] Clinically, ablation threshold for Er:YAG laser has been found to be 1.5 to 1.7 $J/cm^2$for pulses of about 100-microsecond duration.[3-5]

The post-market review

- A substantial volume of literature accompanied the given material on this subject which has been read and assessed but it is impracticable to comment on each individually.
- The common threads in this review are that there is a good deal of marketing rhetoric and precious little, meaningful scientific evidence.
- It is clear that there is a great deal of money to be made should official approval be given to any technique.
- My reading is that the promotion of energy-based equipment as a useful method of so-called vaginal rejuvenation has not yet been substantiated by reproducible, acceptable, scientific evidence.

Questions for ACMD

- *Does the Committee consider that there is sufficient evidence for the use of this kind of device in the treatment of conditions such as vaginal laxity, prolapse, menopausal symptoms, stress urinary incontinence or for improvement in sexual function?* - Insufficient evidence
- *Is the Committee aware of this kind of device being used in Australia, and being generally accepted as the gold-standard option, for any specific treatment pathway?* - Certainly being marketed in Australia. Not generally accepted as the Gold Standard.
- *Is the Committee aware of any other potentially vulnerable patient cohort that may be impacted if regulatory action were to be taken on this kind of device?* Not other than Breast cancer and FGM.

4. *Is the Committee aware of any patient cohorts that may benefit from these devices or treatment options that would be adversely affected if these devices were removed from the market? For example, is this an option for:*

1. *breast cancer patients as a treatment in minimisation of vaginal dryness who may not be able to use hormonal therapies?* Currently insufficient clinical evidence to support.
2. *patients that have undergone genital mutilation, where laser-based devices may be beneficial in the reconstructive procedures?* Currently insufficient clinical evidence to support

Item 5.0

Surgical/dermatological Er:YAG laser system

Device Consulting Pty Ltd

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Erbium Yag laser device in current ARTG

Intended for coagulation, vaporization, ablation or cutting of soft tissue (skin) in dermatology, plastic surgery (including aesthetic surgery), oral surgery and in ophthalmology (skin around the eyes). For the treatment of conditions including acne scars, becker's nevi, café-au-lait spots, elastosis cutis, epidermal nevi (soft), exophytic scars (flat scars, not keloids), lentigines (simplex, senilis), nevi spili, sebaceous adenomas, stepped scars (e.g. camouflage of skin graft borders), syringomas, wrinkles (skin resurfacing), xanthelasmas, seborrhoic keratosis.

Vaginal energy devices Not in ARTG but in IFU

vaginal rejuvenation,

vaginal laxity,

vaginal atrophy,

Genitourinary syndrome Menopause (GSM)

Mild stress urinary incontinence

GSM symptoms include – genital dryness, decreased lubrication with sexual activity, discomfort or pain during sexual activity, post-coital bleeding, decreased arousal, orgasm and desire, irritation/burning/itching of vulva or vagina, dysuria and urinary frequency/urgency.

VVA symptoms include – vaginal dryness, irritation and tenderness, itching and soreness, dyspareunia, vaginal bleeding associated with intercourse, atypical discharge

Vaginal energy devices Contraindications listed

- Injured tissue in the operating room
- Unsolved problems in sexual intercourse. Extremely dry vagina with itching, menopause – hormone treatments
- Strong incontinence
- Active unexplained bleeding or menstruation
- Unknown basin floor problems
- Tendency to hypertrophic scars or keloids (a sample treatment in these cases)
- Not existing of the psychological questionnaire in the run-up to the surgery (patient needs the surgery by itself and not by the insistence of the partner!)
- Pregnancy
- NO MENTION current or Hx recurrent UTI, vaginal infection, abnormal cervical vaginal cystology< vaginal prolapse

Erbium laser claims equivalence Fontana Erbium Laser

Device name	manufacturer	Laser	Wavelength [nm]	Pulse duration [µs]	Pulse-Energy	Spot sizes [mm]
MCL 31 Dermablate Juliet	Asclepion Laser Technologies	Er:YAG Laser	2940	100-1000	1,4	9x9 and 0.4-0.6 mm
Fotona Smooth™ XS IntimaLase™	Fotona, Ljubljana, Slovenia	Er:YAG Laser	2940	50-1500	1,4	2- 7 mm, additional cut handpiece with 0.45 mm (R08-Ti)
Fotona Dynamis PRO IntimaLase™	Fotona, Ljubljana, Slovenia	Er:YAG	2940	100-1500	3	2- 7 mm, additional cut handpiece with 0.45 mm (R08-Ti)

Comment: The Demablate and Fotona Smooth use the same wavelength, the pulse duration and pulse energy fall within the same range however they have different spot sizes.

It unclear whether the difference (upper or lower limit) in the pulse duration could affect the outcome of the treatment.

Application Does not include endorsement of Australian clinical expert gynaecology and LASERs supporting equivalence

Ablative dual-phase Erbium:YAG laser treatment of atrophy-related vaginal symptoms in post-menopausal breast cancer survivors omitting hormone treatment. Mothes 2018

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16 patients

6 week review

94% satisfied

VHI improved post treatment

No adverse events

An innovative dual- phase protocol for pulsed ablative vaginal Erbium: YAG laser treatment of urogynaecological symptoms". Mathes 2018

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84 pre & post menopausal women with urogynaecological symptoms

Single 10 minute laser treatment

6 week review

84% satisfied

Vaginal ph and VHI improved post treatment

Erbium Laser -evidence

No data to prove intervention is effective in treating symptoms

No Data beyond 6 weeks

No data better or worse current treatment (vaginal oestrogens)

Data old from 2018 with only 100 women at 6 weeks re safety

Equivalence to existing Fontana Er Laser not established

Specific advice

Advice from expert – Erbium Yag Laser for Gynaecological conditions has not ben established as effective, safe, equivalent to Fontana device with paucity of data number and duration

Many alternative options available for listed conditions

Specific advice

2. RFA Question 2

Advice from expert – *please provide a brief explanation for your response.*

The response you place here will be copied into the meeting outcome statement (the final version may be varied subject to the discussion of the ACMD).

Any other advice

Any other advice/comments that does not fit under the specific questions?