August 16, 2017

Adjunct Professor John Skerritt, Deputy Secretary,

Mr Tim Greenaway, First Assistant Secretary,

Ms Adriana Platona, First Assistant Secretary,

Ms Cheryl McRae, Assistant Secretary,

Therapeutic Goods Administration, Australia

We are writing this letter from the Urogynaecology Units of Monash Health and Mercy Hospital for Women in response to an invitation to comment on the up-classification of surgical mesh and patient implant cards by the TGA.

In addition, we have become aware of a letter of notice to cancel to Boston Scientific with regard to their female pelvic floor devices, Solyx single incision sling and Uphold lite, and to Coloplast with regard to Altis single incision sling and Restorelle for transvaginal use.

We agree with the up-classification to class III in line with the European regulatory body and the FDA. While the sponsors are providing compliance data, we request the continued availability of single incision slings in the context of clinical studies and in high volume centres, and Uphold and transvaginal Restorelle in clinical studies or in highly specialized units for complex patients. The TGA submission to the Senate Inquiry on transvaginal mesh and related matters noted a four-fold lower complication rate in specialized units.

The European regulatory body has accepted the SCHENIR recommendations in December 2015 and a Consensus Statement of

the European Urology Association and the European Urogynaecological Association (attached) was published in April 2017 that supported midurethral slings and restricted transvaginal mesh to specialised multidisciplinary centres for complex cases. However the European regulatory body did not cancel any devices.

The FDA has called for 522 studies to investigate single incision slings and transvaginal mesh devices rather than cancelling any devices. These FDA studies are currently underway and are at different stages of recruitment and follow-up. For example, the Solyx 522 study is completing its 3 year follow-up over the next months. We have contributed 18 patients to this study and are the only non-US site to be involved.

With respect to single-incision slings for urinary stress incontinence we have strong Australian and international data to support that they are non-inferior with respect to efficacy, and superior with respect to patient-recovery. Single-incision mid-urethral slings are not experimental, they have been available in Australia since 2008 and evaluated in RCT's up to 5 years.

We would like to provide some of the studies which support single incison slings. These include the Melbourne Minimo study, an RCT with published 12 month follow-up (1) and 5 year follow-up presented at IUGA in June 2017 (2). The Dutch group led by Roovers have also conducted a similar comparison with 3 year follow-up with similar success rates and low complication rates.

The 12 month follow-up of RCT, Miniarc vs TVT abbrevo from the Monash Unit was also presented in June 2017 and will be published later this year (3). These two studies were assessing the efficacy of the Miniarc single incison sling. Currently, the two single incision slings available in Australia are the Solyx and the Altis.

As we are a tertiary centre, we are very much involved in contributing high quality research and we are therefore conducting a prospective RCT; a comparison of the Solyx vs the TVT exact retropubic sling for intrinsic sphincter deficiency. Our target is 160 subjects and we have currently recruited 60 subjects; an interim analysis is planned in January 2018. This study as with all others we have conducted, has ethics approval, is registered with ANZCTR and has an independent data safety monitoring committee. It has received research funding from the Australian Bladder Foundation and the Urogynaecological Society of Australasia which lends itself to a process of regular review and compliance.These studies are performed in both the private and public sector. Our understanding is that if the ARTG licence is cancelled, these devices will not receive prosthetic reimbursement which will significantly limit access to women having this treatment in the private sector.

In July 2017, we were granted ethics approval to commence a randomized controlled trial comparing Altis single incision sling with TVT exact midurethral sling in women as there is no published Australian data available on this single incision sling.

Our experience of the Miniarc single incision sling is that it has a lower rate of bladder perforation, bleeding, voiding difficulty and groin pain than retropubic and transobturator slings with similar efficacy. These studies are to determine if the Solyx and Altis which have a very similar sling length, composition and trajectory to the Minarc are also as efficacious as traditional synthetic midurethral slings.

The great majority of women having pelvic organ prolapse surgery for the first time will have a native tissue repair which may or may not include hysterectomy and relies on sutures to suspend or support the uterus or vagina. It has been estimated that up to 15 % or more of women have POP surgery during their lifetime and 10-20 % of those will have repeat surgery. Prolapse recurs more

commonly if it is more severe at the time of the initial surgery or if there has been a pelvic floor muscle tear during childbirth.

We have conducted a patient preference or parallel cohort study comparing Uphold/Uphold Lite with vaginal hysterectomy and are at median follow up of 4 years. This study is being presented in September 2017 at ICS (4). The mesh exposure excision rate after Uphold was 1.8% with equivalent cure rates for prolapse to hysterectomy; the number of overall adverse events was equivalent. This is similar to the results of the Vault trial conducted in the United States which compared Uphold to laparoscopic hysteropexy.(5)The French group has published a large series with low complication rates following Uphold (6).

We do not have experience with transvaginal Restorelle mesh at Monash or Mercy hospitals but have significant experience with Restorelle for sacral colpopexy. Professors Ajay Rane and Alan Lam are part of the 522 study for transvaginal Restorelle. Restorelle is the lightest mesh commercially available at 18.6 g / square metre; for sacral colpopexy it is associated with very low exposure rates and minimal palpability. There are many advantages to Restorelle in laboratory based testing with regard to biocompatibility and decreased stress shielding as reported by Moalli. Transvaginal Restorelle has been associated with < 2% mesh exposure rate at 1 year follow up (Erickson 2011 IUGA abstract)

We understand that the information provided by the Prospect study begun in 2009 and published in 2016 shows there to be no value to mesh inlay reinforcement in primary prolapse surgery at 2 years with an 8% mesh exposure rate. However, this addressed the question of mesh reinforcement in primary surgery which is not current clinical practice and not part of international guidelines.

At IUGA in June 2017, the Prospect 2 study was presented and will be published later this year. This study addressed the role of

native tissue, mesh inlay and mesh kits in recurrent prolapse surgery. The abstract states that 154 women were randomized with 56 to native tissue, 52 to mesh inlay and 46 to mesh kit. At 2 years, there was no difference in subjective symptoms but significantly less objective prolapse in the mesh kit versus native tissue group (0 % vs 17% had leading edge below hymen) however the numbers were too small to be conclusive. The mesh exposure rate at 2 years was 4 women (8.7%) with 2 women (4%) proceeding to surgery to excise mesh exposure. The conclusion of the trialists was that the distinction between primary and secondary surgery should be made in any further studies.

We request the continued availability of single incision slings in the context of an ethics committee approved clinical study or in specialized and high volume units until the TGA is satisfied with the increasing amount of evidence which supports single incision slings. This is consistent with the RANZCOG position statement on midurethral slings.

We would also request the availability of transvaginal mesh in an ethics committee approved clinical study or in subspecialty urogynaecology centres or high volume units where it may be performed after careful counseling in recurrent prolapse as an alternative to repeat native tissue repair or transabdominal mesh. There are clinical scenarios where transvaginal mesh is the preferred option such as recurrence after transabdominal mesh or where transabdominal surgery is not possible or carries a significant risk of bowel injury and morbidity. There is also increasing evidence of a far greater prolapse recurrence risk in women with major pelvic floor muscle trauma (7)

This approach is consistent with the RANZCOG position statement on transvaginal mesh. This surgery could be conditional on compulsory inclusion into the UGSA mesh registry or a registry held by TGA and reviewed on a 6 monthly basis. Indeed,

consistent with an up-classification of all surgical meshes, we would very supportive of a compulsory registry for all of these devices including mesh sacral colpopexy which could be implemented through UGSA which already has a voluntary registry.

We would also be supportive of the provision of a patient implant card and further patient information leaflets. The Monash and Mercy hospitals use those freely available through the IUGA website.

This document has been or is currently being reviewed by the President of RANZCOG, the head of the Urogynaecological Society of Australasia, the Australian Gynaecological Society and Surgical Society, the board of the International Urogynaecological Society and the Functional and Female Urology Special Advisory Group of USANZ and Prof JP Roovers who gave a European urogynaecological perspective. We are submitting this document at this point as we are aware of the date for compliance requirements from the sponsors. The above mentioned societies may choose to provide their own submission.

1. Randomized trial of a single incision versus an outside-in transobturator midurethral sling in women with stress incontinence; 12 month results. Lee,JK Rosamilia,A Dwyer,P Lim,YN Muller,R Am J Obstet Gynaecol. 2015 July; 213(1):35

2. MiniArc Monarc suburethral sling in women with stress urinary incontinence. An RCT. 60 month follow up.Lee J, Rosamilia A, Lim YN, Thomas E, Murray C, Leitch A, Dwyer PL. IUGA June 2017. Attached

3. TVT Abbrevo and Miniarc suburethral sling in women with stress urinary incontinence: A Randomized Controlled Trial. 12 month follow up.Melendez, Braverman, Lee J, Rosamilia

A et al. IUGA June 2017 awaiting publication. Attached

4. Hysterectomy or Uphold Uterine Conservation in women with apical prolapse: a parallel cohort study.
Young N, Leitch A, Ow L, Melendez J, Edwards G, Chao F, Lim Y, Lee J, Rosamilia A, Dwyer P. ICS 2017. Attached

5. Gutman RE, Rardin CR, Sokol ER, et al. Vaginal and laparoscopic mesh hysteropexy for uterovaginal prolapse: a parallel cohort study. Am J Obstet Gynecol 2017;216:38.e1-11.

6. Letouzey V, Ulrich D, Balenbois, Cornille A, de Tayrac R, Fatton B. Utero-vaginal suspension using bilateral vaginal anterior sacrospinous fixation with mesh: intermediate results of a cohort study IUJ 2015 ; 26; 1803-1807

7. Friedman T, Eslick G, Dietz HP. Risk factors for prolapse recurrence- systematic review and meta- analysis. Int Urogynecol J 2017; in print.

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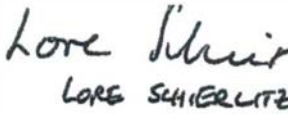

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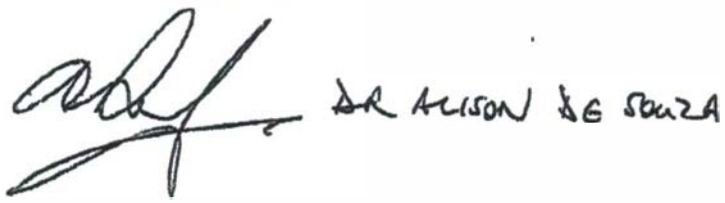

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