

The Independent Medicines and Medical Devices Safety Review

Written Evidence

Other Organisations

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Disclaimer

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WARNING: Please be aware some evidence contains descriptions, pictures and audio of the harm suffered by individuals. Some may find this distressing.

The British Medical Journal

COI: None declared.

Evidence submission regarding pelvic mesh

On 10 October 2018, The BMJ published a series of articles on vaginal mesh.

1. How mesh become a four letter word <https://www.bmj.com/content/363/bmj.k4137>
2. The trial that launched millions of mesh implant procedures: did money compromise the outcome? <https://www.bmj.com/content/363/bmj.k4155>
3. Vaginal mesh implants: putting the relations between UK doctors and industry in plain sight <https://www.bmj.com/content/363/bmj.k4164>
4. Editorial: Surgical mesh and patient safety <https://www.bmj.com/content/363/bmj.k4231>
5. Editor's Choice: What we must learn from mesh <https://www.bmj.com/content/363/bmj.k4254>

Together these present a picture of incompetence, obfuscation, and commercial influence that brings shame on the regulators, clinicians, manufacturers. They show, as outlined in the editor's choice: "that thousands of women have been irreversibly harmed; that implants were approved on the flimsiest of evidence; that surgeons weren't adequately trained and patients weren't properly informed; that the dash for mesh, fuelled by its manufacturers, stopped the development of alternatives; that surgeons failed to set up mesh registries that would have identified complications sooner; and that the National Institute for Health and Clinical Excellence and the UK regulators let them off the hook.

The mesh story also tells us the extent to which surgeons, researchers, and professional bodies are entangled with the device manufacturers.

From this we ask that the Cumberlege review call for:

A mandatory national registry for mesh and all medical devices. The former secretary of state for health, Jeremy Hunt finally set up a prospective comprehensive database for mesh devices in February but there also now needs to be a national recall of mesh with each woman contacted individually so that she can be give a clear idea of her outcome.

Legislation for a US-style Sunshine Act for mandatory open declaration of all doctors' conflicts of interest. The mesh story shows that NHS trusts cannot be left to set up and maintain a publicly-available register of staff interests. The ABPI database is voluntary and therefore ineffective. Patients and the public must be able to access the financial relations of their clinicians. The evidence is clear

that such relations affect the types and extent of treatment given to patients, and the interventions promoted to the public.

Examination of the role of NICE and the MHRA in this health disaster. NICE gave the right warnings about mesh as far back as 2003 but had no power to enforce its recommendations. The MHRA, which is funded by industry, has not led from the front, and has too often fallen back on poor evidence to defend mesh as safe and to preserve the status quo. For journalists and the public, the MHRA represents something of a 'black box'. It's impossible to request information about adverse events related to named devices because the agency pleads commercial confidentiality.

Drug Safety Research Unit (DSRU)

COI:

The Drug Safety Research Trust is a registered independent charity (No. 327206) operating in association with the University of Portsmouth. It receives unconditional donations from pharmaceutical companies. The companies have no control over the conduct or publication of the studies conducted by the DSRU.

1. Please describe the data collection process for Prescription Event Monitoring for drugs, including: study length, cohort size, and whether the information requested can be modified to include pregnancy complications and/or teratogenic effects.

The DSRU conducted Prescription-Event Monitoring (PEM) studies between 1981 and 2011. The DSRU no longer conducts PEM studies, but now uses the Modified PEM (M-PEM) methodology. The main difference between PEM and M-PEM is the specificity and level of detail of the data collection form. Other aspects of the data collection process are common to both methods.

Data Collection Process:

The DSRU notifies the NHS Business Services Authority (BSA) of the drug to be studied. DSRU receives data from DSRU receives data from dispensed primary care NHS prescriptions issued in England by GPs from the date of market launch. A bespoke M-PEM data collection form is sent to the prescribing GP three, six or twelve months after the first prescription for a given patient.

Data collected on an M-PEM data collection form includes the treatment duration, initial dose and dose at event, reasons for stopping, previous medical history, event data during treatment and after stopping, if applicable. Follow-up information is requested from the prescribing GP for events of interest, suspected adverse drug reactions, pregnancies and deaths (where the cause is not specified). The data collection form is designed specifically to collect the precise information required for each study and can be modified to include questions on pregnancy complications and/or teratogenic effects.

M-PEM data collection forms completed by the GP are returned to the DSRU where they are scanned, reviewed and the data entered into DSRU database. The data is analysed and a study report written.

Medicines studied using M-PEM methodology are typically widely used drugs used for common indications. An M-PEM cohort may be up to 10,000 patients.

The DSRU is supported by the Marketing Authorisation Holder (MAH) while conducting a M-PEM for their product M-PEM study. However the DSRU is independent and impartial and does not endorse any drugs. Nearly all M-PEM studies conducted by the DSRU recently are part of the regulatory requirements for risk management.

M-PEM is explained in more detail in this publication, which is submitted with this response:

Layton, D., Hazell, L. & Shakir, S.A. Modified Prescription-Event Monitoring Studies: A Tool for Pharmacovigilance and Risk Management. Drug Safety (2011) 34: e1-e9.

2. What actions do the DSRU take following the identification of adverse events by Prescription Event Monitoring?

All M-PEM study reports are sent to the MHRA and EMA, as well as the Marketing Authorisation Holder for the medicine. Any adverse events identified during M-PEM would be submitted to the MHRA and EMA in one or more interim reports, as well as the final study report.

Any unexpected or serious adverse events detected during M-PEM would be reported within the required regulatory period to the MAH to be reported to the relevant medicines regulator.

3. How can adverse event data reporting and sharing be improved internationally?

Eudravigilance provides a platform for sharing data within the EU. It is feasible to expand this system to a wider international network.

4. Do you hold any archive material relevant to the interventions under Review?

No, the DSRU has not conducted studies on hormone pregnancy tests, sodium valproate or synthetic mesh. However the DSRU has conducted studies on approximately 120 medicines using PEM, M-PEM or the equivalent methodology for hospital prescribing ("SCEM"). A list of the drugs we have studied can be found at <https://www.dsru.org/past-studies/>

Besides these event monitoring studies in primary and secondary care, the DSRU also conducts drug utilisation studies, risk minimisation studies, CPRD studies, European network studies and registry studies.

5. What would you consider to be the defining features of an effective clinical registry? Who is best placed to host such a registry? How can healthcare professionals be encouraged to use the registry?

Registries are formal repositories of information, the data entry is structured. Registries can be used to conduct a range of observational studies, e.g. cohort, case-control or cross-sectional studies depending on the question(s) that need to be answered. Registries can be disease based or product based. The Drug Safety Research Unit in Southampton (DSRU) has the capabilities (both data management infrastructure and scientific) and a successful track record to build and conduct registries (disease, medicines or devices registries).

We confirm that we give permission for this evidence to be used for the purposes of the Review.

Drug Safety Research Unit, October 2018