Drug recall procedure in United Kingdom and Australia: a regulatory overview

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ABSTRACT
Recall occur as a consequence of the safety concerns over a manufacturing defect in a product that may harm its user. Due to their deficient quality, security or effectiveness, medicinal products are accused of being possibly dangerous to customers and may be subject to recall. A recall is defined as the process of recovering. A pharmaceutical product from the distribution chain due to product deficiencies, complaints of serious adverse reactions or corners that the product is or may be defective. The objective of study is to help identify the significance of the recall action and classification and focused on the prospective danger of the patient / consumer defect and, to understand the recall procedure in United Kingdom and Australia. The recall may either be conducted by the license holder or the manufacturer, or and the wholesale dealer. The evaluation should consist of checking the efficacy of the recall and investigating the justification for the recall as well as the remedial measures adopted to avoid the occurrence of the issue. The present work highlights the comparison of the recall procedure between United Kingdom and Australia.

INTRODUCTION
In Australia Recall is defined as, A product recall is done to safeguard the safety and security of customers from medicinal products and some of those may get an impact by a problem with a medicinal good, with respect to

1. Safety or security
2. Efficacy (drugs and biologics)
3. Performance (medicinal device)
4. Analysis
5. Quality (does not include the grade of products or manufacture for recall reasons).

These problems may be due to non-compliance with defined norms, legislative or manufacturing specification or the relevant therapeutic goods (Rajput, 2020).

Pharmaceutical products and substance that are, or may be, unsafe in their production or packaging. It refers to all medicinal products and thus includes authorized and unlicensed products (including non-licensed medicinal products imported and special) experience demonstrations that it can be difficult to distinguish among defects, mistakes and adverse drug reactions.

To avoid these complexities, an adequately skilled and experienced healthcare professional should initially evaluate a suspected faulty medicinal product. The pharmaceutical sector in managing and
researching alleged deficiencies in quality. It provides information of both the legal demands and the expectations of MHRA with regard to complaints, inquiries and recalls linked to product quality. It applies to all licensed producers and wholesaler, including those handling unlicensed goods, as well as holders of marketing authorization (Recalls and Australian Government. Department of Health Therapeutic Goods Administration, 2020).

The country profile of United Kingdom and Australia with its parameters based on capital, population, area, language and currency and regulatory authority MHRA and TGA. Table 1 shows country profile of the both countries (Recalls, 2020).

**DISCUSSION**

The drug product recall of United Kingdom and Australia are described in Figure 1, (Rajput, 2020). The drug recall classification for United Kingdom and Australia shown in Table 2. As per class 1 to 4 and class 1 to 3 respectively for both the countries (Wagner and Súilleabháin, 2020).

**Recall procedure in United Kingdom**

Recalling Defective Medicinal Products After consultation between the DMRC and the license holder, the decision to recall a product or batch is made in almost all cases. While the MHRA has legislative powers to require a recall, these are rarely used, as long as license holders operate with the MHRA openly and closely (Recalls, 2020). Once a choice has been made to recall a batch or product batches, a number of additional choices must be made. Table 3, shows recall classification of United Kingdom as per class I to IV (MHRA, 2020).

**The Responsibilities of Distributors**

Figure 2, Shows responsibilities of distributors (MHRA, 2020).

**Healthcare Professionals’ Responsibilities**

Figure 3, Shows the healthcare professionals responsibilities (MHRA, 2020).

**Follow-Up – The Licence Holder and the DMRC**

1. The license holder should draw its own conclusions about a suspected flaw and submit the appropriate supportive information to the DMRC

2. If the license holder is uncertain of their findings, they must consult the DMRC for guidance.

3. The DMRC professional staff will then assess, refer to other MHRA experts if necessary, and advise the license holder whether they promote their decision, if additional questions need to be answered, or if alternative or additional action is required.

4. The inquiry is only closed when the DMRC issues a closing reply when a formal inquiry is conducted.

5. The license holder should provide periodic updates on the advancement of the recall inquiry.

6. In the longer term, a final report should be submitted no later than 12 weeks after the initial report for a period to be agreed with the DMRC, unless otherwise agreed.

7. Regardless of the system used, the license holder will need to provide periodic updates on the advancement of the recall to the DMRC.

8. These reports should include a summary reconciliation between the quantity of the item on the market and the quantity returned up to the reporting date.

9. A percentage that should be expected to be returned cannot be specified because this will differ based on the specific conditions of a recall.

10. A final report will be required to close the recall after a period agreed with the DMRC (Nahon, 2018).

**Recall procedure United Kingdom**

The following flow chart describes stepwise recall procedure for recall of drug products in United Kingdom as shown in Figure 4. (Wood, 2016).

**Recall procedure in Australia**

1. From step 1 Immediate Recall

2. Recall begin from step 1, because no sooner than usual it is critical of the Australian recall coordinator and clients.

3. The flow chart shows who (and what in order) needs to be contacted for each case. Make sure that the remaining steps are followed after this original portion of recall procedure shown in Figure 5. (URPTG, 2020)

**Step 1. Immediate recalls**

1. Immediate and serious threats and manipulation
Table 1: Country Profile

| Parameter               | United Kingdom                          | Australia                             |
|-------------------------|-----------------------------------------|---------------------------------------|
| Country name            | United Kingdom of Great Britain         | Common wealth of Australia             |
| Capital                 | London                                  | Canberra                              |
| Largest city            | London                                  | Sydney                                |
| Population              | 62.8 million                            | 22.9 million                          |
| Area                    | 242,514 sq. km (93,638 sq. miles)       | 7.7 million sq. km (2.9 million sq. miles) |
| Major language          | English                                 | English                               |
| Major religious         | Christianity                            | Christianity                          |
| Currency                | Pound sterling (1-pound sterling = 94 INR) | Australian dollar (1 Australian dollar = 52 INR) |
| Government              | Unitary parliamentary constitutional monarchy | Federal parliamentary constitutional monarchy |
| Regulatory authority    | Medicines and Healthcare products Regulatory Agency (MHRA) | Therapeutic Goods Administration (TGA) |

Figure 1: Drug product recall of different countries regulatory authority
Table 2: Classification of drug recall

| United Kingdom | Australia |
|----------------|-----------|
| 4 Classes      | 3 Classes |
| Class I - Life threatening. | Class I - Most serious safety-related. |
| Class II - mistreatment or harm to patient. | Class II - Urgent safety-related. |
| Class III - unlikely to cause harm to patient. | Class III - Lowest risk. |
| Class IV - “caution in use” called class IV drug alert. | |

Table 3: Classification of recall in United Kingdom

| Class | Deficiency                                                                 | Recall procedure                                                                                                                                 |
|-------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Class I | The deficiency poses a life-threatening or severe health threat. | Recall should be patient level; however, if alternate medicine is not accessible, it may not be suitable to carry out an evaluation of the general danger to patients. License holders may need to organize press releases and advertising campaigns. |
| Class II | The deficiency may cause maltreatment or damage to patient, but it is not life-threatening or severe. | Patient level are rarely needed for this level of danger and recall may pose a higher danger to the patient than continued therapy Reminder levels. |
| Class III | The deficiency is improbable to affect the patient, and the recall is performed for other purposes, such as marketing non-acceptance. | Recall can only be made to the level of the supplier in situations where stocks are improbable to appear further supply chain and the risk level is low enough. |
| Class IV | The MHRA also issues alerts of “Caution in use” that are called Class 4 Drug Alerts. So, if an MHRA Drugs Alerts is granted, as suggested at the early part of the preceding sentence, the license holder is still responsible for the recall. | MHRA’s action is secondary to and supports the license’s action. Where patients are not threatened or no severe defects are likely to impair the use or effectiveness of the item. Where an alert is needed, the Agency will operate with the license holder. |

Recall procedure

1. Unsafe radiopharmaceuticals or defective products
2. Unsafe or faulty biologics, parts of human blood and blood product
3. Unsafe radiopharmaceuticals or defective products
4. Unsafe or faulty biologics, parts of human blood and blood product

Recall procedure

1. Step 2 - Finding stock and distribution status
2. Step 3 - Risk analysis assessment
3. Step 4 - Level of recall, class, type determining
4. Step 5 - Recall strategy developing
5. Step 6 - Communication procedure drafting
6. Step 7 - Recall information submission
7. Step 8 - Evaluation of recall by TGA
8. Step 9 - Recall implementation
9. Step 10 – Reporting the recall
10. Step 11 – Recall review

Step 2 finding stock and distribution status

As a sponsor of a recall or non-recall intervention, receive data on:
Completing the rest of the recall procedure steps
Assure that any public health and safe hazards have been efficiently mitigated

**Identify the problem**
Provide all appropriate information on the therapeutic good problem and type including:

1. Issuing date are identified
2. Photographs showing the problem
3. Occurring of problem are identified
4. History of the event, including any reported patient injuries with particular dates and times when it happened was observed.
5. Known issues or comparable issues that happened in the past

**Details of distribution and inventory status of the products concerned include**

1. Releasing date
Figure 4: Recall Procedure flow chart in United Kingdom
2. Batch quantity releasing
3. Product distribution to Australian market date and amount or quantity of product
4. Distribution chain place
5. Complete quantity supplying to consumers
6. Countries from which the goods are exported

**Step 3 Risk analysis assessment**

1. Analyse the hazards connected with the therapeutic good impacted as the sponsor. To assist determine the sort of recall or non-recall, step 4 is required

The level of recall class determines the types and class of recall in Australia shown in Figure 6.

**Step 5. Recall strategy developing**

The following recall strategy includes:

1. Details of product in the recall
2. The problem, including the prospective hazard or risk assessment of the products
3. The type, classification and recall level suggested as set out in step 4
4. Specifics known injury or incident involving the products or goods

Communication details of:

1. Sponsor
2. Other entities in the supply chain who supply the goods
3. International recipients if appropriate of exported products

**Step 6: Communication procedure drafting**

Communication strategy content include:

1. If the products were exported, a description of the expected customer in Australia and other nations are communicated.
2. Methods to communicate with supply chain operators

**Step 7: Recall information submission**

1. Distribution information and inventory status
2. From step 3 risk assessment
3. From step 4 recall level, class and type
4. Step 5 recall strategy

**Step 8: Evaluation of recall by TGA**

**Analyzing risk**

1. Conduct an autonomous and objective evaluation to check that the approaches are suitable for mitigating the hazards posed by the products concerned.
Evaluating the strategy for recall

1. Evaluate the work closely with the recall and to provide guidance and assistance regarding letters, commercials and strategies for recall.

Option to order a recall

1. Appropriate recall strategy to reach agreement with. The function is to safeguard public health and safety and can mandate reminder if needed.

Time frame to report

1. Within seven working days, the time frame is to react and process a recall, but generally accomplish this in less time. Review and prioritize all notification upon receipt.

Step 9: Recall implementation

A reminder for sponsor

1. Implement strategies for communication and recall once it is agreed

Sending the Customer letter

1. Sending the customer letter from the sponsor

Recovery of impacted products once the recall strategy has been agreed

1. Recovery arrangements for the products
2. Set collection points throughout the distribution network

Consumer follow up

1. It is essential that client follow-up is carried out to guarantee that they have obtained and followed the client letter direction
2. The amount of monitoring will rely on the risk and recall class.

Step 10 – Reporting the recall

1. Generate detailed reports using the letter of contract provided by the templates. Reports should be adequate to analyse the efficacy of the step 11 recall.

Step 11 – Recall review

The recall review process in Australia is designated in Figure 7 as shown (Emmerig et al., 2019).

Recall action type

1. Type of the Recall
2. Alteration of product imperfection
3. Aware for hazard
4. Alert for the product fault

Recall class

1. Class I- serious of product related to safety
2. Class II – urgent security
3. Low risk
Table 4: Classification of recall in Australia

| Class   | Recall Conditions                                                                 | Examples                                                                                       |
|---------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Class I | A situation where there is a fair likelihood that the use or contact to the lacking therapeutic goods will result in severe negative health or death effect. | Counterfeit medicine, chemical contamination, microbial injection or ophthalmic sterile contamination, counterfeit active ingredient in multi-component medicine. |
| Class II| A situation where the use or exposure to the deficient therapeutic goods may trigger negative health effects that are temporary or medically reversible or where the likelihood of severe negative health effect is low | Mislabelling, missing or inaccurate safety data in insert or wraps, mixing in containers of medicinal products. |
| Class III| A situation where the use or exposure to the deficient therapeutic goods is unlikely to cause negative health effect. | Incorrect packaging, such as incorrect or missing lot number or expiry date, closure of containers |

The classification of recall in Australia as per Class I, II, III is shown in Table 4. And described in detailed (Recalls and Australian Government. Department of Health Therapeutic Goods Administration, 2020).

Four level of recall are:

1. Wholesale level
2. Hospital level
3. Retail level
4. Consumer level

**Wholesale level**

1. Wholesale of medicines and medical device who hold products to be distributed to distributors or other organization
2. Purchasing officials of the state and territory

**Hospital level**

Healthcare facility, nursing homes.

**Retail level**

1. Hospitals
2. Dentist
3. Retail pharmacy

**Consumer level**

1. Hospital, retail level

2. Consumers and patient

**Non-recall act**

Not all problems involve action to be considered.

On-recall are conducted if:

1. The therapeutic products comply with all requirements and norms
2. There are no safety, quality, effectiveness, performance or presentation deficiencies

**Customer letter from the sponsor for recalls**

The client letter from the sponsor is the component of the recall procedure and is a factual declaration of the reasons for the recall along with particular information for easy identification of impacted product (TGA, 2020).

For Class I and Class II recalls

1. Recall of urgent medicine
2. Medicine Recall
3. Medical Device Recall
4. Biologicals Recall
5. Mandatory recalls

The mandatory recall offence and penalty for offence has shown in Table 5. Fine ranging from 1000-4000 Penalty (Guidelines for Product Recall and Product Withdrawal-First edition, 2006).
### Table 5: Mandatory recall offence and penalty

| Offence                                                                 | Recall penalty                                                                 |
|------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Punished with a crime Officine and the court finds himself guilty of the offense | 1. Imprisoned for up to twelve months or 5 years if no recall in damage or injury to individual  
2. Fines ranging from 1000 – 4000 penalty                                |
| Also, civil fine procedure conducted on them in a court, and if the court discovers the violation that have been committed | 1. Civil penalties are ordered to pay |

### CONCLUSION

The recall of the product consists of well-established written procedures and systems to record, access, investigate and review the potential quality defects to safeguard the public health from the low quality or damaged products. The recall of the medicinal product should be controlled by the regulatory authority, enforcement and should understand the identification of nature of recall action and classification based on potential risk the deficiency poses to patients or consumer and it should be controlled. the regulatory authority, enforcement, inspection should control the recall of the product.

### Conflict of Interest

The authors presenting the paper and entitled “Drug Recall Procedure in United Kingdom and Australia” does not pose conflict of interest.

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