Product Recall - Risk Assessment

Recall - Background

Product recall is a key area of risk for today's company

- With greater focus on, and understanding of the impact of products and their raw materials on individuals, systems and the environment, the ability to manage the product throughout its lifecycles is essential
- Supply and distribution chain visibility are essential to managing product safety and may ultimately reduce the likelihood of major recalls

Those companies that have

- spent the time to understand the recall risk in advance, and
- have a defined and tested process in place

are far better prepared to cope with the unexpected when it does happen, and minimize the potentially negative consequences to the company's reputation.

➔ **So, how does a company go about assessing the recall risk for its products?**

Why Is it essential ?

With risk analysis

- **Understand**
  - the recall risk in advance, and
  - have a defined and tested process in place,

  are far better prepared to cope with the unexpected when it does happen

- **Minimize** the potentially negative consequences to the company's reputation

A well managed risk assessment will enable the definition of an encompassing process that if needed, will not only show the company as responsive, efficient, and prepared, but also may highlight corporate responsibility and good citizenship.

Risk Assessment - Methodology

- A risk assessment can only give a snapshot of the risks at a particular point in time.
- Recall risk assessment should be a frequent activity, comprehensive risk assessment should be conducted at least once every two years to explore
  - the risks associated with the organization's products.
  - A key component of all risk assessments should be the relevant and constantly changing regulatory requirements.
- The progressive company is now including recall risk assessment contingency planning with all new and upgraded product rollouts.

Why Risk Assessment ?

To analyzes the relationships between : Risk (severity), assets, threats, vulnerabilities, impacts and other elements.

Many methodologies, in general they can be classified into two main types: **quantitative** and **qualitative** analysis.

- **quantitative** analysis
  - the **impact of the risk and the effect of** the recall issues,
  - together with some qualitative statements describing the significance and the appropriate measures for minimizing these risks.

- **qualitative** analysis
  - analyzing the **likelihood of the** event occurring.

Risk Assessment - Methodology

- **Impact Assessment**

  (also known as Impact Analysis or Consequence Assessment)

  - estimates the degree of the overall harm or loss that could occur as a result of a recall.
  - quantifiable elements of impact are those on revenues, profits, cost, service levels, regulation and reputation.
  - it is necessary to consider the level of risk that can be tolerated and how, what and when assets could be affected by such risks.
  - the more severe the consequences of a threat, the higher the risk. An example of this would be: a recall on a product that is found to have an unacceptable breakage level where the consequent pieces are benign is a lot different to one where the pieces do not pass the infant choking hazard standard.

Risk Assessment - Methodology

- **Likelihood Assessment estimates the probability of a threat occurring.**
  - In this type of assessment, it is necessary to determine the circumstances that will affect the likelihood of the risk occurring.
  - The likelihood can be expressed
    - **in terms of the frequency of occurrence**, such as once in a day, once in a month or once in a year. The greater the likelihood of a threat occurring, the higher the risk.

      It can be difficult to reasonably quantify likelihood for many parameters; therefore, relative likelihood can be employed,

    - **as in a ranking**. An illustration of this would be: the relative likelihood of a product piece to detach, or a catastrophic failure of a key control mechanism.

To Recall or not to Recall?

What Manufacturers and Product Retailers Must Keep in Mind When Something Goes Wrong

To Recall or not to Recall?

The decision to recall a product must be made with regard to the risks of the defective products.

1. The Initial Analysis

- The first step is to carry out urgent due diligence on the product and its defect to identify the nature and extent of the risk.
- Often the trigger to commence this process is a customer compliant or a notice from Regulator – Health Authority
- The analysis process will include liaising with internal management and the parties who are involved in producing the product. Also, it is prudent to engage independent experts to provide their report and recommendations.

To Recall or not to Recall ?

2. Risk Assessment

Having conducted the initial analysis, the next stage is to carry out a risk assessment in order to decide whether the defect is serious enough to warrant a recall of the product.

Risk assessment usually has several phases:

- **Identifying the hazard**
  This involves identifying the nature and cause of the hazard, what range of products and who is affected by it and whether there are any factors that could affect the severity and probability of injury.

- **Estimating the level of risk**
  Estimating the risk depends on two main factors: the severity and the probability of possible injury to a person.

- **Estimating the acceptability of risk**
  To decide whether you need to take action, you also need to assess whether or not the level of risk is acceptable to consumers.

To Recall or not to Recall ?

2. Risk Assessment

- **Overall risk**
  Having evaluated all these factors you should make an overall risk assessment, which may be expressed as one of the following levels

  - **Serious risk ➔ requiring rapid action**
  - **Moderate risk ➔ requiring some action**
  - **Low risk ➔ not generally requiring action for products on the market**

To Recall or not to Recall ?

3. Taking Corrective Action

The decision regarding the type of action to take will mainly be dependent on the overall level of risk.

a. If the overall level of risk is judged to be serious, immediate action should be taken:
   - Inform the market surveillance authorities
   - Isolate stocks
   - Ask distributors and retailers to isolate affected products
   - Inform suppliers of any affected components
   - Set up a communications program to contact and information consumers
   - Collect and destroy products in the marketplace

b. If consumers can be traced, then they can be contacted directly. If not, then appropriate notices will be required, including in newspapers, on the internet and/or with retailers. The notices must clearly identify the affected products and set out clear instructions to the consumer.

To Recall or not to Recall ?

c. If the overall level of risk is judged to be moderate, the corrective action may be limited to products in the distribution chain only, including:
   - Withdrawing them from the distribution chain
   - Rectifying the defective component
   - Issuing revised instructions and/or components to consumers and retailers
   - Improving the product in design and production
   - Improving the instructions supplied with a product

d. If the overall level of risk is judged to be low, corrective action may generally be limited to considering changes in design and production.

The Extent of Recall

- Having decided a recall is required, it will then be necessary to determine how comprehensive the recall needs to be.
- A full recall will usually involve:
  - A stop on production and delivery, withdrawal of stock from shelves, returns to the producer and destruction of the affected products
  - Direct communication with traceable consumers, point of sale recall notices in retail outlets and after-sales service centers, press releases and publication of recall notices in the press
  - Informing the relevant authorities
  - Setting up a free telephone help desk, instructing a PR agency and solicitors

Learning from Experience

- **Manufacturer side**
  - If a certain was at fault for the defect, then an internal review should be carried out in relation to all products produced by that manufacturer.
  - Quality assurance certificates for all products should be regularly updated and, in particular, a review should be carried out in relation to not only the manufacturer, but also the issuer of the quality assurance certificates in order to pre-empt problems.
- **Regulatory point of view**
  - should learn how to asses the RISK and its analysis process, in getting complete data or picture to take a final decision prior to requesting a RECALL.
  - it will be also very valuable to engage independent experts to provide their recommendations concerning the RISK LEVEL and its impact

Product Recall Risk Assessment

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  - A comprehensive risk assessment should be conducted at least once every two years to explore the risks associated with the organization's products.
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Product Recall Risk Assessment

- The Risk Assessment approach is particularly applicable when many disciplines of the company are directly involved in a process.
- It enables many voices and viewpoints to be heard, and a more inclusive and complete process results.
- For a product recall many constituencies are likely involved, including :
  - ✓ Safety
  - ✓ Customer service
  - ✓ Accounting
  - ✓ Supply chain
  - ✓ Public relations, etc.

Regulasi yang terkait dengan *Recall*

Indonesian GMP – CPOB 2012
CHAPTER 9
HANDLING OF PRODUCT COMPLAINTS AND PRODUCT RECALLS

Penarikan Kembali Obat Jadi

Prosedur Tetap / Protap

* *Personel yg bertanggung jawab*
* *Team Penarikan kembali obat jadi dng tanggung jawab masing-masing*

Pelaksanaan :
- *Sesegera mungkin setelah diterima laporan tentang produk yg cacat mutu atau adanya laporan yg merugikan*
- *Disertai dengan embargo, sesuai kebutuhan*
- *Prosedur harus menjangkau ke tingkat konsumen*
- *Pemeriksaan kembali harus cepat, efektif & tuntas*

Dokumentasi :
- *Catatan distribusi*
- *Pemberitahuan penarikan kembali obat jadi*
- *Rekonsiliasi hasil pemeriksaan*

Penanganan Produk :
- *Identifikasi & status*
- *Terpisah dari produk lain & terperinci*
- *Penanganan lebih lanjut*

Mock Recall :
- *Evaluasi efektifitas prosedur penyelenggaraan penarikan kembali obat jadi*

Tindakan lanjutan recall :
- *Pengumpulan dan evaluasi data di laboratorium*
- *Pengumpulan dan evaluasi data proses termasuk kajian resiko mutunya*

Tindak lanjut Recall oleh Industri Farmasi

EVALUASI CEPAT TINDAK LANJUT RECALL

Voluntary recall

- Penyimpangan berasal dari hasil stabilitas on-going / pasca pemasaran , technical complaint dan non compliance izin edar
- Investigasi HULS ? Alat , Metoda analisis, personil , reagen
- Investigasi diminta dengan melihat data trend yang didapat dari PQR → **tidak hanya** melihat 1 bets yang ditemukan cacat mutu
- Hasil TMS terjadi berulang ,
  - Lihat di catatan pengolahan bets → ada penyimpangan ?
  - Bandingkan dg Reg dossier yang disetujui → perubahan formula , perubahan sumber bahan awal , proses ?
- Review protap → diperbaiki sebagai tindakan preventif

TINDAK LANJUT RECALL

Mandatory recall

- Dalam hal mandatory recall , BPOM mengirim surat perintah kepada pemilik izin edar untuk melakukan ,
  - Penarikan obat yang TMS
  - Investigasi penyebab obat TMS → ***hasil investigasi bisa MS atau TMS***

→ BPOM melakukan *evaluasi hasil investigasi pemilik izin edar*

EVALUASI CEPAT TINDAK LANJUT RECALL

Mandatory recall

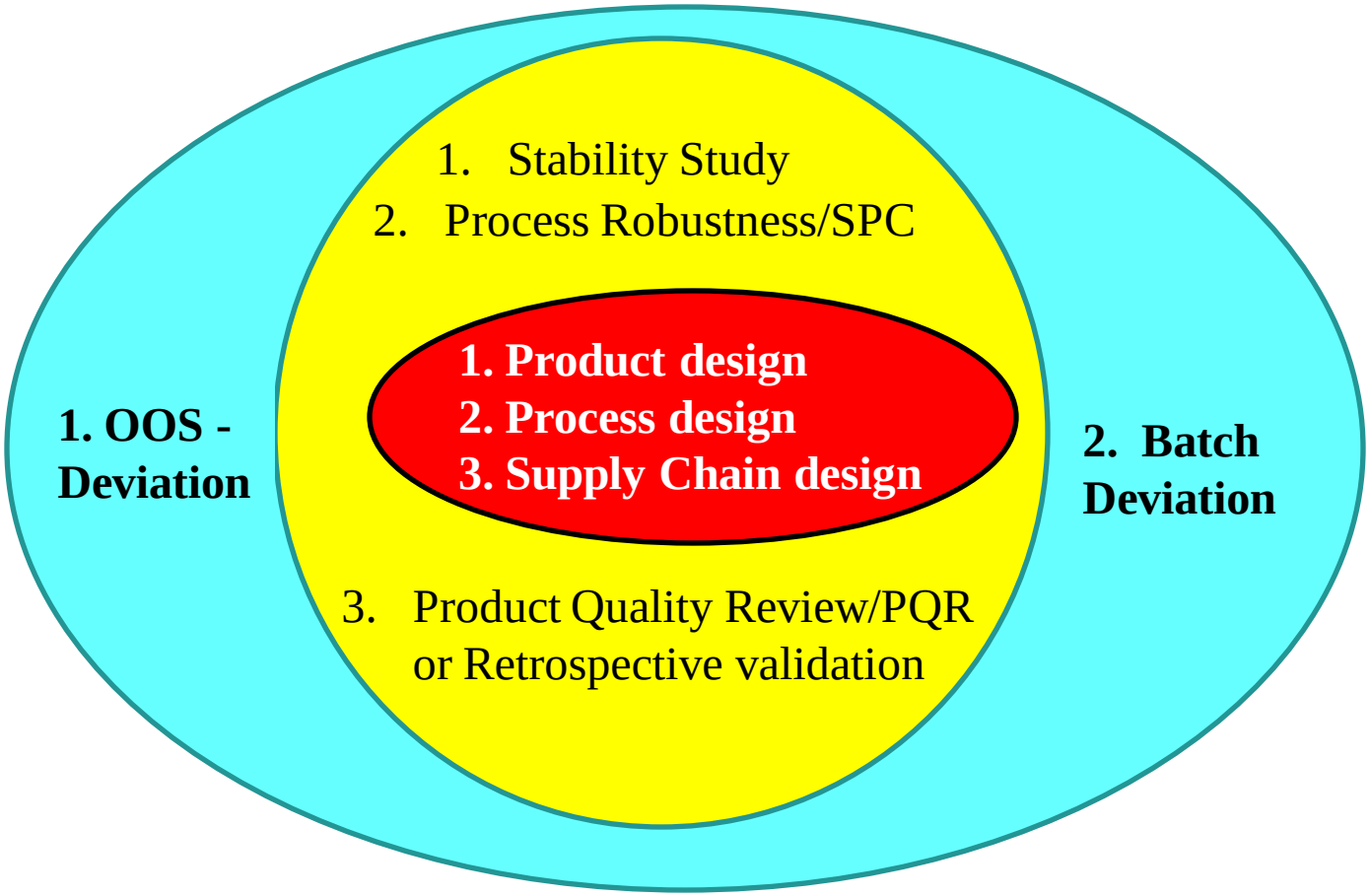
- Evaluasi Hasil investigasi
  - Penyimpangan yang ditemukan oleh BPOM→ berupa HULS
  - Investigasi HULS ? Alat , reagensia , Metoda analisis dan personil
  - Atensi untuk Referensi MA → di industri rata2 memakai USP , BP dengan edisi yang mutakhir (requirement dari Ditlai pada saat registrasi , ketentuan di CPOB) vs PPOM yang masih banyak referensinya mengacu FI IV dan/ addendum FI IV

EVALUASI CEPAT TINDAK LANJUT RECALL

Mandatory recall

- Evaluasi Hasil investigasi
  - Investigasi juga diminta melihat data trend yang didapat dari PQR → **tidak hanya** melihat 1 bets yang ditemukan cacat mutu
  - Jika dari PQR juga ada hasil TMS dari spesifikasi yang sama yang terjadi berulang mis. disolusi , pH , kadar dan belum ada tindakan perbaikan dari industri terhadap produk terkait maka hasil investigasi yang MS tidak dapat diterima
  - Tidak perlu dilakukan uji bersama

Kajian tindak lanjut



Cause and Effect/Fishbone Diagram

Find and Cure causes, NOT symptoms

- To Identify, Explore and Graphically display, in increasing detail, all of the possible causes related to a problem or condition ➔ to discover its ROOT CAUSES
- Focus :
  - On the content of problem, not on the history of the problem or differing personal interest of team members
  - On causes, not symptoms

Pilih format CAUSES – EFFECT yang paling sesuai

a. **Dispersion Analysis Type - DAT**
   - Placing indifidual causes within each **“major” cause category**,
   - kemudian tanya setiap individu, individual cause :
     - KENAPA PERSOALAN/CAUSE ini TERJADI ?
   - Ulangi pertanyaan tersebut untuk setiap level detail sampai tidak bisa lagi mendapatkan jawabannya.

b. **Process Classification Type - PCT**
   - Uses the **“major” steps of the process** in place of the major cause categories.
   - Tanykan setiap induvidu, individual cause
     - KENAPA PERSOALAN/CAUSE ini TERJADI ?
   - Ulangi pertanyaan tersebut untuk setiap level detail sampai tidak bisa lagi mendapatkan jawabannya.

Deviation

OOS = Out Of Specification

- Reportable result that falls outside established specifications or acceptance criteria on the drug master file, approved marketing submission, compendia or internal specification
  - This does not include situation where the control test is not continued due to violation of SST limit or identification of gross operator errors during the run e.g. wrong instrument setting

OOT = Out of Trend /Atypical Test Result /Aberrant/Anomalous Result

- Analytical result, which is still within specification but different /unexpected, questionable, irregular, deviant or abnormal from those usually obtained or expected
  - OOT should be investigated by the same general principles as OOS results

Analytical (Laboratory) error

- Analytical (laboratory) error can be instrument or operator e.g.
  - injection/instrument error,
  - mistake in following the method analysis
  - wrong sample preparation
  - use incorrect standard
  - wrong instrument setting,
  - transcription or calculation error

Others ➔ improper or uncompleted data – limited information – inaccessible data

Principles and Methods

The primary objective of a OOS investigation and assessment is to determine, whether or not a failure, of the analyte that is being tested has occurred

The activities should be :

- Starting with data, information, and solution already present
  - **Initial Laboratory Investigation = ILI ➔ covering Phase Ia and Ib**
- If no analytical error can be identified, the investigation proceed to additional experimental studies e.g.
  - **Full Scale OOS Investigation ➔ covering Phase II and III**
    - Full laboratory Investigation
    - Production Review
- Performed in a systematic, well structured and stepwise approach
  - Risk Analysis

Note :

- If an analytical error is identified as the cause, the original OOS result can be invalidated
- As far as possible, Corrective and Preventive Actions should be identified and implemented in order to prevent re-occurrence of such errors

私はすべてがうまくいくよう願ってる
Watashi wa subete ga umaku iku yō nega~tsu teru

どうもありがとうございました ….

Domo arigatogozaimashita

Terima kasih