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Lääkealan turvallisuus- ja kehittämiskeskus | Säkerhets- och utvecklingscentret för läkemedelsområdet | Finnish Medicines Agency

GMP-tilaisuus 3.5.2012

Riskien hallinta – mitä kokemuksia käyttöönotosta Suomesta ja maailmalta

EU GMP-Guide viitteet

- EU GMP Guide, Chapter 1, Principle
- To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance incorporating Good Manufacturing Practice, Quality Control and Quality Risk Management. It should be fully documented and its effectiveness monitored.

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EU GMP Guide Part I: 1.5 ja 1.6

- 1.5 Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and retrospectively.
- 1.6 The quality risk management system should ensure that:
- - the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient
- - the level of effort, formality and documentation of the quality risk management process is commensurate with the level of risk

- Examples of the processes and applications of quality risk management can be found inter alia in Annex 20.

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QRM (Quality Risk Management) - PIC/S

- PIC/S Aide Memoire PI 038-1, 26 March 2012 on ilmestynyt - löytyy http://www.picscheme.org/
- tarkastusten apuväline:
  - Millä tasolla riskinhallinnan käyttöönotosta ollaan
    - Onko ohjeistettu?
    - Onko olennainen osa laadunhallintaa/laatupolitiikkaa?
    - Onko järjestelmällistä?
    - Onko johdon tuki näkyvästi olemassa?
    - Miten käytännössä näkyy toiminnassa?
      - Henkilökunnan koulutus riskinhallintaan
      - Tuotteiden laaturiskit kartoitettu ja arvioitu systemaattisesti asiantuntevien henkilöiden toimesta
      - Riskejä valvotaan, seurataan ja niistä kommunikoidaan asianmukaisesti

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Odotukset laaturiskinhallinta käyttöönotosta mm. seuraavilla alueilla

- Poikkeamien käsittely
- Valitusten ja tuotevirheiden käsittely, takaisinvedot
- Muutosten hallinta
  - Uudet tuotteet ja prosessit
  - Menetelmien ja tuotteiden siirrot
  - Tilojen ja laitteiden muutokset
- Näytteenottomenetelmät ja analysointi
- Validoinnit ja kvalifioinnit
- Kalibroinnit ja ennakkohuollot
- Toimittajien kvalifiointi, raaka-aineiden toimitusketju
- Auditointiohjelma
- Jne.

- *Laaturiskin hallinnassa odotus on, että potilasriskejä ja lääkkeen laaturiskejä arvioidaan, vähennetään ne hyväksyttävälle tasolle sekä että niitä seurataan. Yrityksen tulee viedä valvontajärjestelmänsä sille tasolle, että tuotteen laatu ja potilaan turvallisuus ovat optimissaan. Kustannusten lasku ei voi olla ensisijaisena tavoitteena riskinhallinnalle GMP:n näkökulmasta*
- *Riskien hallinnan tulee olla jatkuvaa! - esim. ovatko alkuperäiset riskien hallintaan liittyneet päätökset olleet riittävät, vai tuleeko niitä muuttaa*

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Tarkastushavaintoja riskinhallintaan liittyen (Fimea - PIC/S maat):

- *Risk management was not an essential part of company quality policy*
- *There was no procedure or policy describing company's approach to QRM*
- *There was no risk register to facilitate the management, monitoring and review of formal risk assessments. There were numerous and significant changes to processes, equipment and facilities which may impact on decisions or outcomes of previous risk assessments or mitigation strategies.*
- *Risk Management was not implemented to handling of deviations, complaints and product defects.*
- *Procedures for complaints and deviation handling did not include risk assessment and consideration of extending investigation to other batches*

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Tarkastushavaintoja riskinhallintaan liittyen (Fimea - PIC/S maat):

- *The company's approach and risk assessments for preventing cross contamination were not evident, incomplete and did not include all relevant manufacturing areas and products*
- *Lack of risk assessment following technology transfer of productX, so provide assurance that containment measures were adequate to minimise impact on other products manufactured in the facility.*
- *Risk of cross-contamination was not formally assessed*
- *There was no formal risk assessment conducted to determine the scope and extent of validation, e.g. critical steps and the extent and amount of sampling*

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Tarkastushavaintoja riskinhallintaan liittyen (Fimea - PIC/S maat):

- *(Environmental Monitoring- Aseptic Production) The risk assessment for the justification of sample locations was based upon an assessment of the existing locations, rather than an assessment of the criticality of each graded area and the activities undertaken within*
- *Placement of settle plates was not justified by risk assessment*
- *The environmental risk assessment written to justify the current monitoring positions had failed to identify potential risk areas such as …(examples)*

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Tarkastushavaintoja riskinhallintaan liittyen (Fimea - PIC/S maat):

- *"Your firm has not established separate or defined areas or such other control systems as necessary to prevent contamination or mix-ups during aseptic processing. [21 C.F.R. § 211.42(c)]. For example,*
  *a) Your firm lacked an adequate **assessment** of the **cross-contamination risks** posed by the manufacture of several potentially hazardous compounds (e.g., beta lactam antibiotic and steroid products) at your facility. Deficiencies were observed in the shared manufacturing areas where you manufacture potentially hazardous compounds and sterile ophthalmic drug products intended for the U.S. market. You should ensure that a documented justification and a well-designed contamination prevention strategy has been put in place to minimize the possibility of contamination. **FDA encourages sound risk assessment approaches to address hazard identification, exposure consequences, and implement controls designed to prevent and detect cross-contamination**. To achieve an **acceptable level of risk requires sound and risk-based assurance** that one drug does not contaminate another drug."*