THE RISK-BASED APPROACH TO MONITORING

Bénédicte Votan – GCIG Chicago 2015 – Harmonization session

WHAT IS IT ?

- **Guidance** developped by FDA in August 2013 to assist sponsors of clinical investigations in developping risk-based monitoring strategies and plans for investigational studies

GOAL OF THIS GUIDANCE

- **To enhance patient protection** and **quality of clinical trial data** by focusing sponsor oversight on the most important aspects of study conduct and reporting

WHY THIS GUIDANCE HAS BEEN DEVELOPPED ?

- Changes in the number and complexity of clinical trials (increase) ➔ New challenges to clinical trial oversight

  - Variability in clinical investigator experience
  - Variability in site infrastructure

  ➔ monitoring should be adapted

WHY THIS GUIDANCE HAS BEEN DEVELOPPED ?

- Limitations of on site monitoring

= is inadequate to ensure patient safety and quality

ie : even with on site monitoring risks to subjects can be missed or responded to in an untimely manner

WHY THIS GUIDANCE HAS BEEN DEVELOPPED ?

- Increasing use of electronic systems and records present opportunities for alternative monitoring approachs (centralized/ remote monitoring)

➔ We (sponsors) have to adapt and to take advantage of the new technologies to improve monitoring

HOW TO USE THIS GUIDANCE

1 – To assess the projects risks and needs

- Complexity of the trial, risk for the patient new drug…

2 – To adapt the monitoring in relation to the risk of the trial

- Low risk = remote monitoring
- High risk = on site monitoring at regular intervals

HOW TO USE THIS GUIDANCE

3 – Focus on the most critical data elements

4 – Adjust the monitoring strategy according to the analysis of ongoing data

➔ This approach is totally different from traditional method with planning prospectively monitoring visits

CONCLUSIONS

- The FDA believes that targeted risk-based approaches that focus on the most critical data elements will result in more effective monitoring

- Both FDA and EMEA encourage sponsors to adopt strategies that reflect a risk-based monitoring approach using a combination of monitoring strategies and activities

THE RISK-BASED APPROACH TO MONITORING

The PAOLA-1 example

PAOLA-1 study

- International, phase III, registration study
- Level of monitoring= high (on site + remote monitoring)
- Monitoring adapted in relation to the site and the quality of the site and adjusted on an ongoing basis :
  - On site initiation visit for all sites
  - First monitoring visit in all sites within 3 weeks after enrollment of first patient

PAOLA-1 study

- After the first visit, the state of the site is defined as :
  - Green site : 100% compliant with protocol and requested documentation
  - Orange : some minor deviations during the site visit (minor deviation should be defined in advance in the monitoring plan)
  - Red : significant deviations

PAOLA-1 study

- The on-site monitoring visits are then adapted to the state of the site
  - **Green** : next monitoring visit in 4 months
  - **Orange** : next monitoring in 3 months
  - **Red** : next monitoring in 6 weeks

Each monitoring visit redefines the state of the site to schedule the next visit

PAOLA-1 study

Between the visits :

- Remote monitoring 1/month
- Following each remote monitoring, in case of suspected major risk the visit of monitoring can be advanced

THANK YOU FOR YOUR ATTENTION !