EIPG General Assembly

Industry Implications of Pharmaceutical Quality ICH Guidelines

20th April 2008

presented by John DR Jolley

Pharmaceutical Quality

“ Develop a harmonised pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science.”

Q8: Pharmaceutical Development

Q9: Quality Risk Management

Q10: Pharmaceutical Quality System

Pharmaceutical Development.

The aim of pharmaceutical development is to design a product and its manufacturing process to consistently deliver the product conforming to the intended performance.

The information and knowledge gained in the pharmaceutical development studies and manufacturing experience provide scientific understanding to support the establishment of the design space (QbD) , specifications and manufacturing controls.

ICH Guidelines Pharmaceutical Development continued

To achieve the desired state;

- Product quality and performance should be achieved and assured by design of effective/robust manufacturing processes.
- Product specifications should be based on mechanistic understanding of how formulation and process factors impact on product performance,
- Product quality and performance linked to clinical safety and efficacy.

ICH Guidelines- Quality Risk Management

To provide the principals and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality in development, manufacturing, distribution and inspection.

Principals of Quality Risk Management

- Foundation for science based decisions when integrated in to quality management systems.
- Can facilitate better and more informed decisions
- Can provide regulators with greater assurance of companies ability.
- Can facilitate better use of resources.

Quality Management System.

All licensed medicines must be manufactured so as to ensure that they are fit for the intended use and do NOT place patients at risk due to inadequate safety, quality or efficacy.

To achieve the quality objectives their must be a comprehensive QMS incorporating Good Manufacturing Practice and Quality Control.

There are additional legal responsibilities for the designated Qualified Persons (QP) to control the release of products compliant with MA.

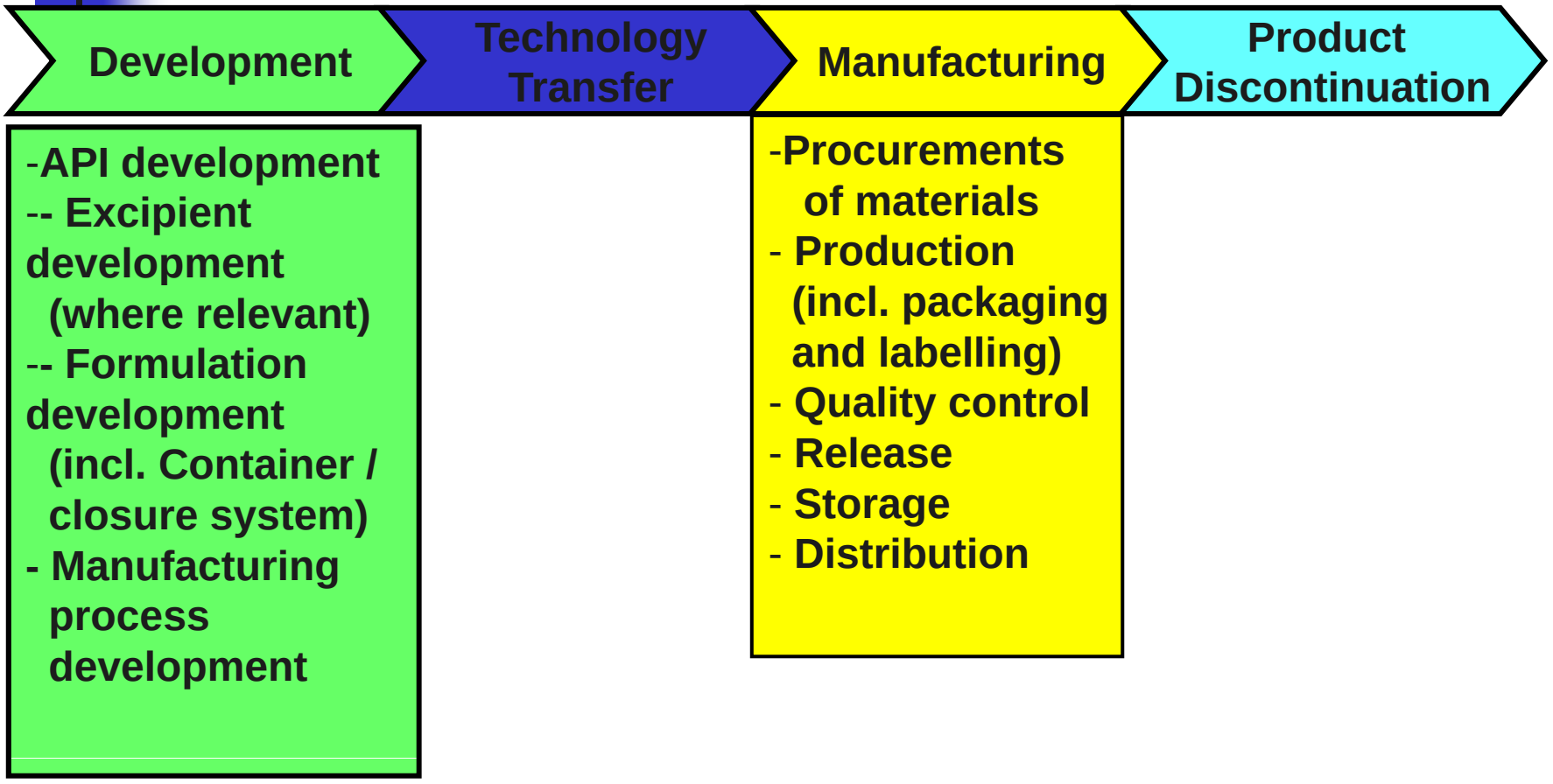
Pharmaceutical Quality system: Introduction

1. ICH Q10 describes a comprehensive approach to an effective pharmaceutical quality system for the pharmaceutical industry
2. It is based on ISO concepts, includes applicable Good Manufacturing Practice (GMP) regulations and complements ICH Q8 “Pharmaceutical Development” and ICH Q9 “Quality Risk Management”
3. It can be implemented throughout the different stages of a product lifecycle.

Q10 implementation status

- Transmission to CHMP and to Interested Parties May 2007. Issued as EMEA/CHMP/ICH/214732/2007. Deadline for comments: November 2007
- Comments will be discussed in an ICH meeting in Spring 2008 with the goal to reach step 4.
- Step 2 of the document reached during ICH meeting in Brussels (5-10 May 2007)

Definition of Product life cycle



Composition of the document

The document is divided in 5 sections and one annex

1. The Pharmaceutical Quality System
2. Management responsibility
3. Continual improvement of process performance and product quality
4. Continual improvement of the pharmaceutical quality system
5. Glossary
6. Annex 1 concerning potential opportunities to enhance science and risk based regulatory approaches

Composition of the document

1. The Pharmaceutical Quality System :Scope

- This guideline applies to pharmaceutical drug substances and drug products, including biotechnology and biological products
- The elements of ICH Q10 should be applied in a manner that is appropriate and proportionate to each of the product lifecycle stages, recognizing the differences among, and the different goals of each stage.

Composition of the document

1.The Pharmaceutical Quality System : scope

For the purposes of this guideline, the product lifecycle includes the following technical activities for new and existing products :

- Pharmaceutical development
- Technology transfer
- Manufacturing
- Product discontinuation

Composition of the document

1.The Pharmaceutical Quality System : scope

ICH Q10 Objectives

- ☞ Achieve product realisation
- ☞ Establish and maintain a state of control
- ☞ Facilitate continual improvement

Composition of the document

1.The Pharmaceutical Quality System : scope

Two enablers have been mentioned in this document (knowledge management and quality risk management) that facilitate a consistent scientific approach to achieve the objectives of Q10.

Composition of the document

2.Management responsibility : key elements

This part of the document is really based on ISO norms (series 9000) and describes :

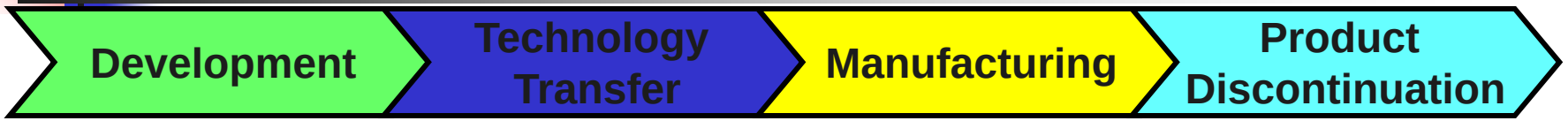
- ☞ Management commitment
- ☞ Quality policy
- ☞ Quality planning
- ☞ Resource management
- ☞ Internal communication
- ☞ Management review
- ☞ Oversight of outsourced activities

Composition of the document

3. **Continual improvement of process performance and product quality : key elements**

This section describes, for each of these 4 elements, what can be done for each step of the product lifecycle, notably through tables.

Knowledge Management-Monitoring



Development	Technology Transfer	Manufacturing	Product Discontinuation
Can be utilised to identify critical process parameters and critical quality attributes	Confirms the suitability of the process and the successful transfer into manufacturing	Should be applied ***Knowledge gained to be incorporated into the knowledge management system*** Output should be an input to each of the other PQS elements	Measurement of the process ceases Monitoring of e.g. stability studies continues Where warranted action on marketed products must still be executed

Composition of the document

4.Continual improvement of the pharmaceutical quality system

This section describes activities that should be conducted to manage and continually improve the pharmaceutical quality system.

Continual improvement of process performance

Principal components of PQS :

- Process performance and product quality monitoring system
- Corrective Action and Preventive Action System (CAPA)
- Change management system
- Management review of process performance and product quality

Composition of the document

5 Glossary

- ☞ This section provides definition used into ICH Q10
- ☞ ICH and ISO definitions are used where they exist
- ☞ Where no ICH or ISO definition was available, an ICH Q10 definition was developed

Composition of the document

5 Glossary

☞ Pharmaceutical Quality System : management system to direct and control a pharmaceutical company with regard to quality. (ICH Q10 EWG based upon ISO 9000-2005)

☞ Control strategy : a planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10 EWG)

Composition of the document

5 Glossary

☞ Enabler : a tool or process which provides the means to achieve an objective. (ICH Q10 EWG)

☞ State of control : a condition in which the set of controls consistently provides assurance of continued process performance and product quality. (ICH Q10 EWG)

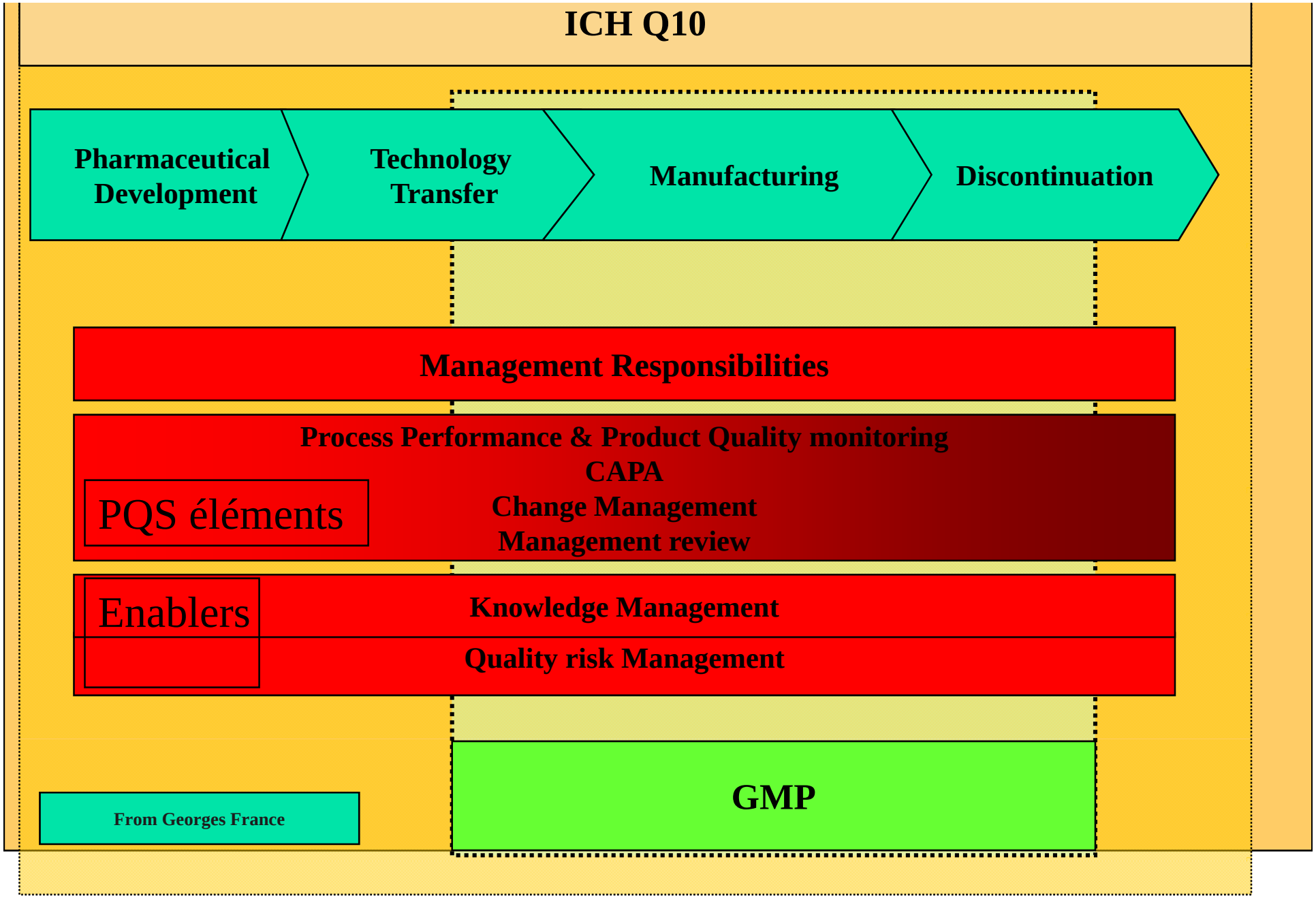
☞ Senior management : person (s) who direct and control a company or site at the highest levels. (ICH Q10 EWG based on ISO 9000-2005 definition for “Top Management”)

Composition of the document

6 Annex 1 concerning potential opportunities to enhance science and risk based regulatory approaches

☞ This section describes 4 different scenarios considering implementation or not of ICH Q8, Q9 and Q10 documents and envisages potential opportunities which could occur

☞ The actual regulatory process will be determined by region



presented by John DR Jolley

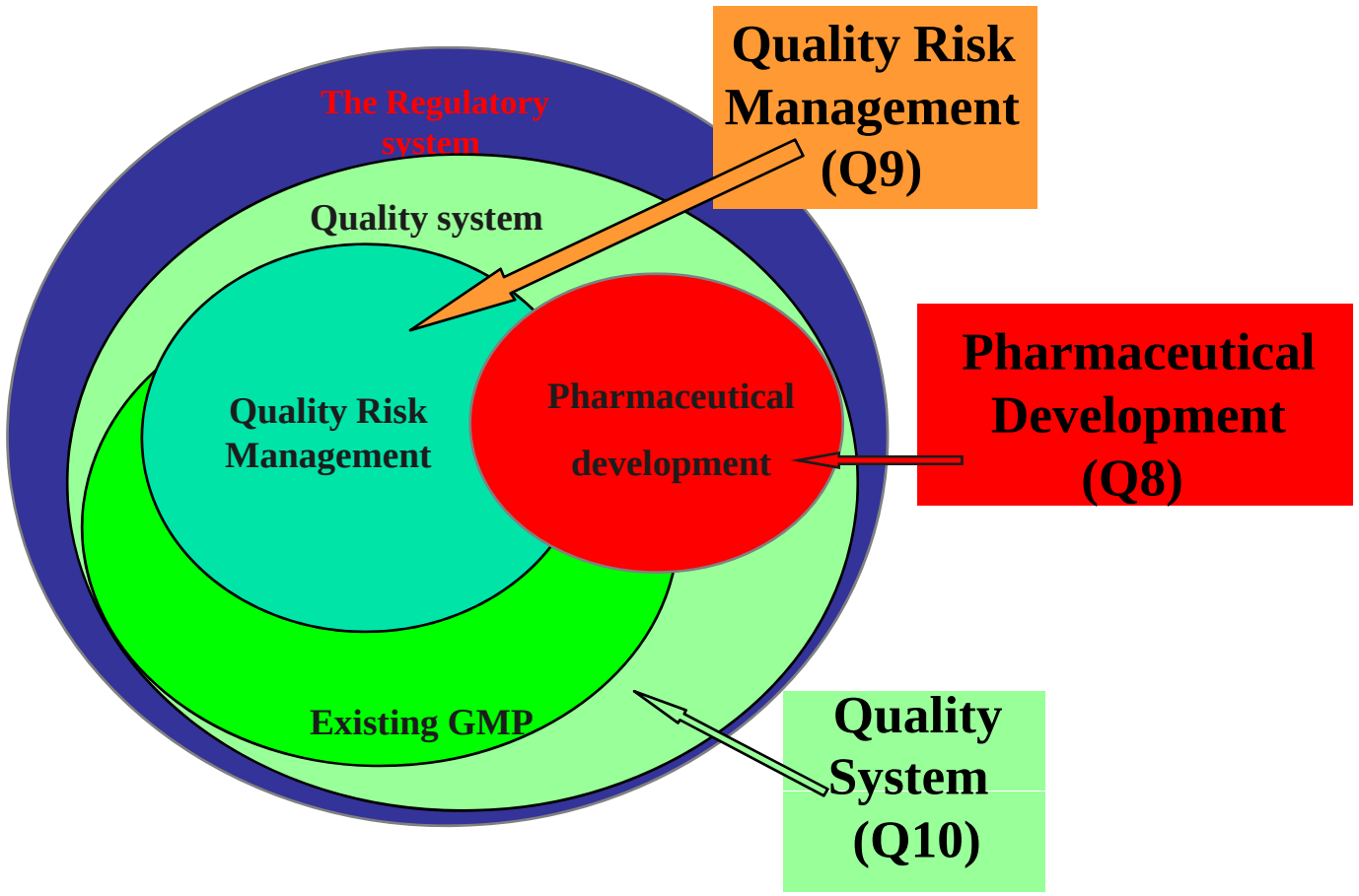
Conclusion

- This document is **one** model for implementing a PQS throughout the different stages of a product lifecycle.
- Implementation of Q10 as described in annex 1 should conduct to potential opportunities
- This document is product related and not system related
- Which is different from current GMP
- And complicates the understanding of the document

Conclusion

- ☞ This document facilitates the implementation of ICH Q8 and Q9 but can be used independently from them
- ☞ It could be used only for one (or more) step(s) of the product lifecycle
- ☞ When implemented, the effectiveness of the pharmaceutical quality system can normally be confirmed during a regulatory inspection

Quality Management systems-Scope



presented by John DR Jolley

Thank you for your attention

- Any Questions