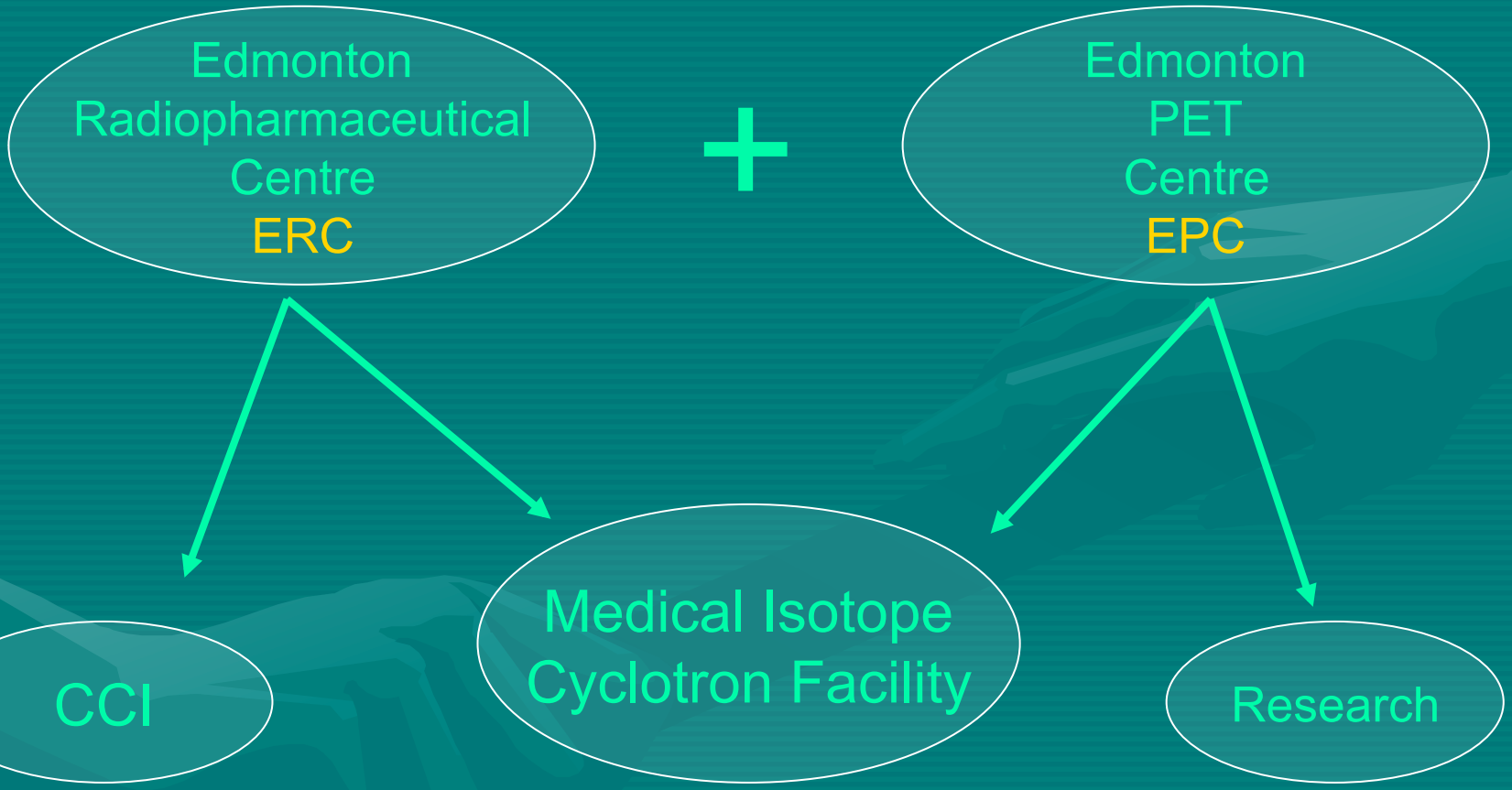
Business Continuity during build & after move monitoring of risk and quality management reference to ICH Q9

Douglas N Abrams,
University of Alberta,
Medical Isotope Cyclotron Facility

OR
Maintaining quality in the midst of chaos

Project


Edmonton
Radiopharmaceutical
Centre
ERC
+
Edmonton
PET
Centre
EPC
CCI
Medical Isotope
Cyclotron Facility
Research

Cross Cancer Institute

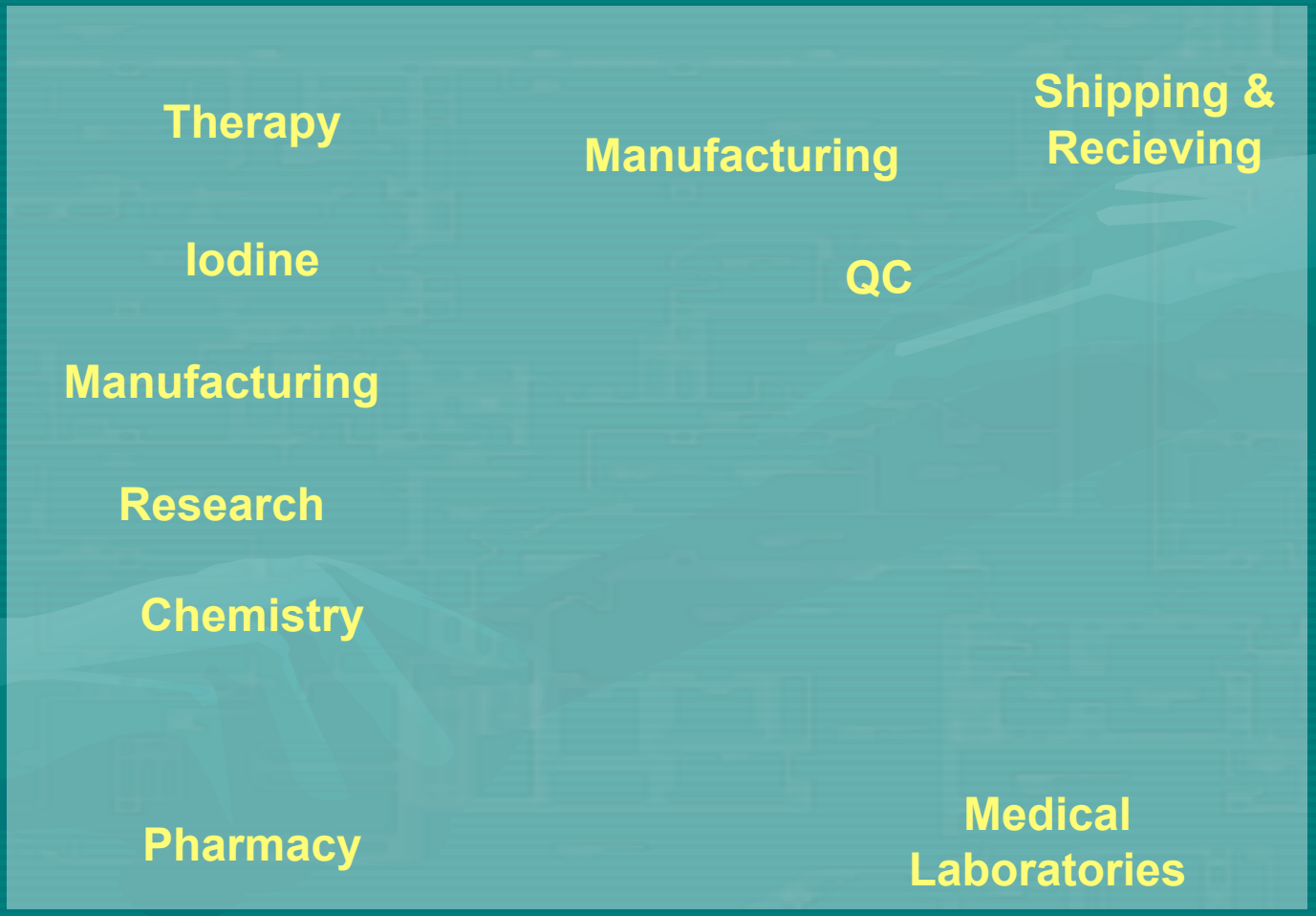
CBIAR

Edmonton PET Centre

Oncologic Imaging
Nuclear Medicine

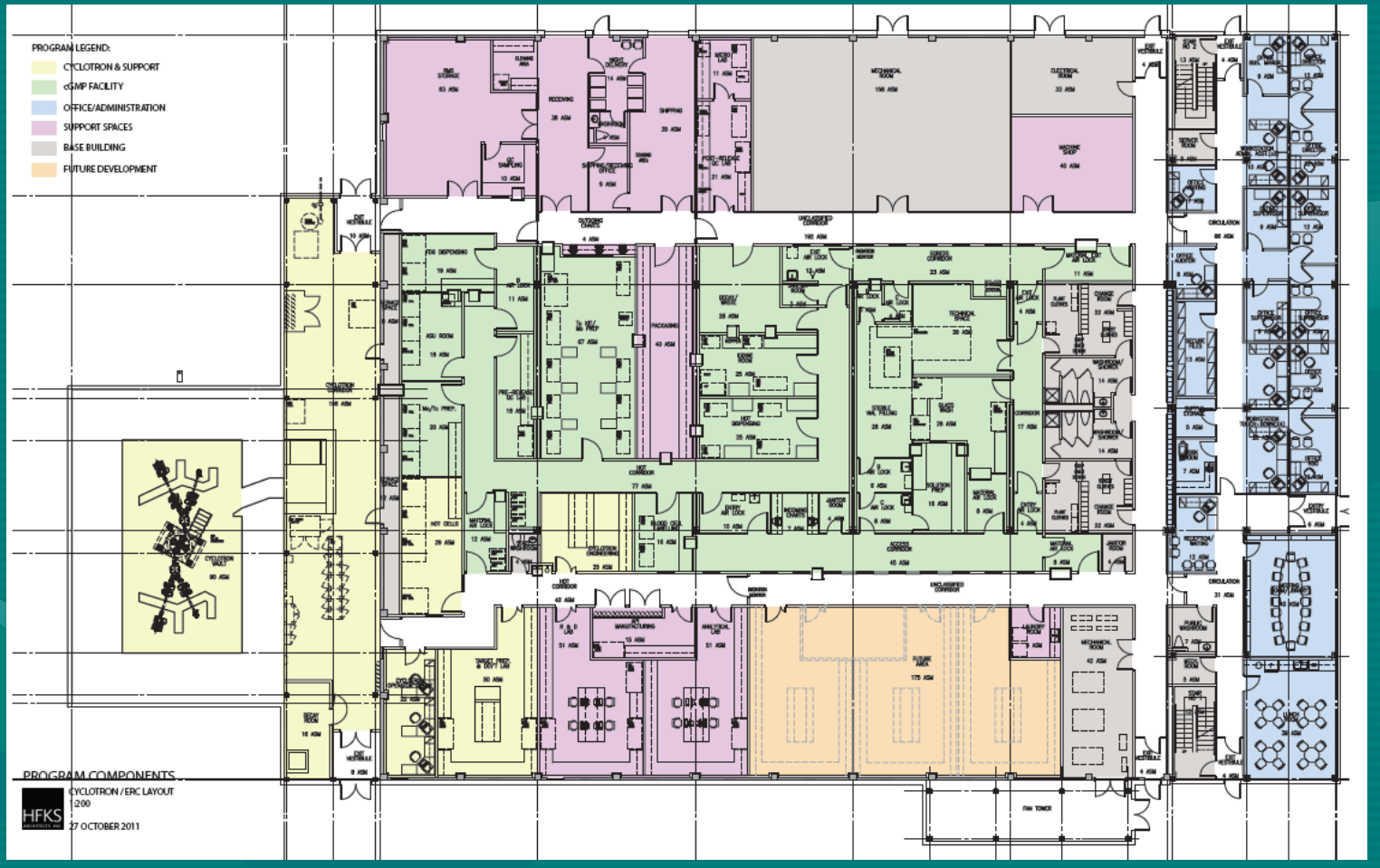
Edmonton Radiopharmaceutical Centre

Edmonton PET Centre

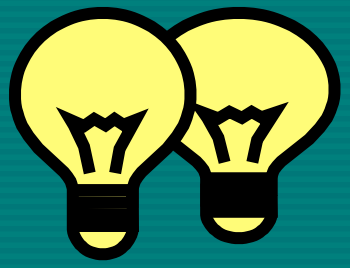


Edmonton Radiopharmaceutical Centre

Medical Isotope Cyclotron Facility



Why did we do this?



Dated/Tired Facility

Tc-99m Shortage

ACSI
Sherbrooke

Edmonton

Cyclotron

U of A
Scientists

Balmoral Project

S McEwan
S McQuarrie

D Abrams

Medical Isotope
Cyclotron Facility

What does this mean?

MICF

1. Cyclotron
   1. F-18
   2. Tc-99m
   3. I-123
   4. ?
2. Radiopharmaceutical Preparation
3. Kit Manufacture
4. API Manufacture
5. CT RP Preparation
6. UofA Research
   1. Basic
   2. Clinical Trials

EPC

1. Cyclotron
   FDG
   Research PERs
2. UofA Research
   1. Basic
   2. Clinical Trials

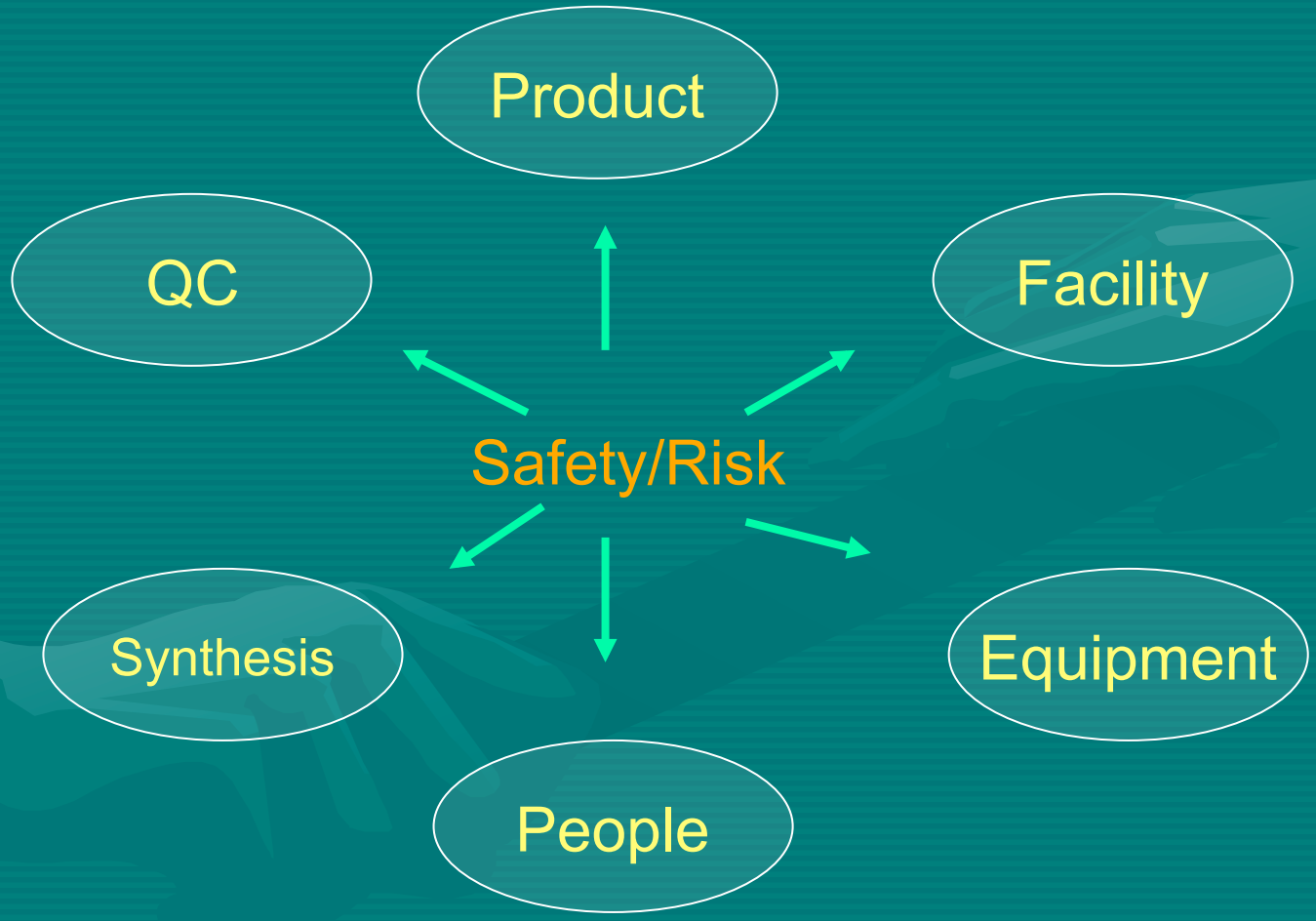
ERC

1. Purchase RNs
2. RP Production
3. Kit Manufacture
4. API Manufacture
5. CT RP Preparation

What does this mean?

Don't Underestimate
the Challenges
or
the Opportunities

Risk Management



Introduction

Radiopharmaceuticals are somewhat unique in the pharmaceutical world

they cannot be stockpiled in the usual manner in anticipation of a disruption in supply due to a move or facility renovation

Introduction

Therefore
Radiopharmaceuticals must continue to be manufactured
during a move
or renovation of a facility

Managing the risk of two separate operations
simultaneously impacts staffing and resources

ICH Quality Risk Management Q9

- Is based on risk management principles
- Are used in other areas of business and government
- Are used by regulating agencies

- Are hard copy identification of common sense (conceptually vs implementation)

ICH Quality Risk Management Q9

How does ICH Q9 fit in?

Does not deal with Radiopharmaceuticals explicitly
Rather
it is an all encompassing document for pharmaceuticals

Risk Management

These principles address risk in preparing

drug substances,

drug (medicinal) products,

biological products

biotechnological products

Including the risk associated with the use of

raw materials,

solvents,

excipients,

packaging and labeling materials

ICH Quality Risk Management Q9

Defines *risk* as
the combination of the *probability*
of occurrence of *harm*
and
the *severity* of that harm.

Risk Management

The systematic application of quality management

policies, procedures, and practices

to the tasks of

assessing, controlling, communicating and reviewing risk.

Words of Encouragement From ICH Q9

So far the constant theme has been somewhat daunting
regulation, regulation, regulation
however Q9 offers some words of encouragement.

Communication
Degree or Rationalization of Risk
Degree of Formality and Effort

ICH Q9
Communication

While regulatory decisions will continue to be taken on a regional basis, a *common understanding* and application of quality risk management principles could *facilitate mutual confidence* and *promote more consistent decisions* among regulators on the basis of the same information.

This *collaboration* could be important in the *development of policies and guidelines* that integrate and support quality risk management practices.

Canadian Experience
Communication

Regulatory decisions continue to be taken on a case by case basis, to form a *common understanding* and application of quality risk management principles to *promote more consistent decisions* among regulators on the basis of the same information.

This *collaboration has* been important in the *development of policies and guidelines* to support clinical trials and facility development.

Canadian Experience
Communication

Canada has recognized that RPs are a bit of a different entity and that there is a need and there has been very good cooperation between the regulators both drugs directorate and the inspectorate

Workshops

December 2012 theme was New RPs and Alternates to Tc-99m

December 2013 theme is Harmonization of the Inspectorate

ICH Q9
Rationalization of Risk

In relation to pharmaceuticals,

the protection of the patient by managing the risk to quality should be considered of prime importance.

The manufacturing and use of a drug (medicinal) product, including its components, necessarily entail some degree of risk.

ICH Q9
Management of Risk

It is neither always appropriate nor always necessary to use a formal risk management process (using recognized tools and/ or internal procedures e.g., standard operating procedures).

The use of informal risk management processes (using empirical tools and/ or internal procedures) can also be considered acceptable.

Appropriate use of quality risk management can facilitate but does not obviate industry's obligation to comply with regulatory requirements and does not replace *appropriate communications between industry and regulators.*

ICH Q9
Management of Risk

Principles of quality risk management are:

- The evaluation should be based on scientific knowledge
- The level of effort, formality and documentation should be commensurate with the level of risk.

Break Time

Count the "F"s in the following sentence

FINISHED FILES ARE THE RESULT OF YEARS OF SCIENTIFIC STUDY COMBINED WITH THE EXPERIENCE OF YEARS

Risk Assessment

1. What might go wrong?
Risk identification

2. What is the likelihood (probability) it will go wrong?
Risk analysis

3. What are the consequences (severity)?
Risk evaluation

Risk Control

decision making to reduce the risk to an acceptable level.

- Is the risk above an acceptable level?
- What can be done to reduce or eliminate risks?
- What is the appropriate balance among benefits, risks and resources?
- Are new risks introduced as a result of the identified risks being controlled?

Risk management should be an ongoing part of the quality management process.

Risk Reduction

focuses on processes for mitigation or avoidance of quality risk

improve the detectability of hazards

implementation of risk reduction measures can introduce new risks or increase the significance of other existing risks.

revisit the risk assessment to identify and evaluate any possible change in risk after implementing a risk reduction process.

Risk Acceptance

even the best quality risk management practices might not entirely eliminate risk.

In these circumstances, it might be agreed that quality risk is reduced to a specified (acceptable) level.

should be decided on a case-by-case basis. g

Risk Control Tools

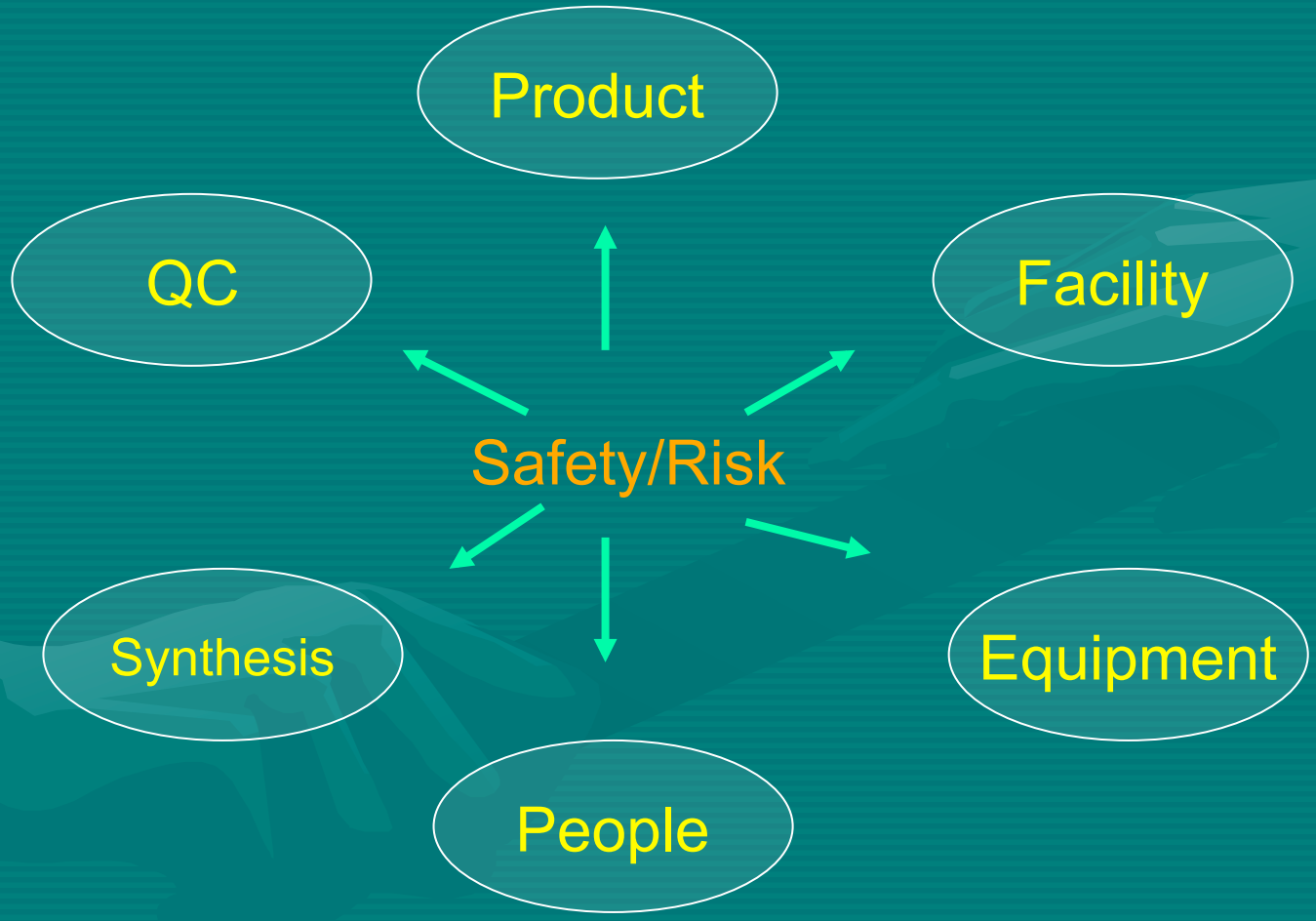
- Basic risk management facilitation methods (flowcharts, check sheets etc.)
- Failure Mode Effects Analysis (FMEA)
- Failure Mode, Effects and Criticality Analysis (FMECA)
- Fault Tree Analysis (FTA)
- Hazard Analysis and Critical Control Points (HACCP);
- Hazard Operability Analysis (HAZOP);
- Preliminary Hazard Analysis (PHA);
- Risk ranking and filtering;
- Supporting statistical tools.

Risk Program Integration

can provide regulators with greater assurance of a RP's ability to deal with potential risks,

might affect the extent and level of direct regulatory oversight.

Risk Management



Risk Management

Current Operation

1. Facility
    1. Environmental Control
    2. Functional Control
2. Equipment
    1. Environmental Control
    2. Functional Control
3. Process
    1. Product Quality Control
4. Personnel
    1. Qualification
5. Documentation
    1. Review

New Operation

1. Facility
    1. Environmental Validation
    2. Functional Validation
2. Equipment
    1. Environmental Validation
    2. Functional Validation
3. Process
    1. Product validation
4. Personnel
    1. Qualification
5. Documentation
    1. Generation

Facility

Current Operation

1. Current Personnel
2. GMP Microlab

New Operation

1. Commissioning Team
   1. UofA
   2. Contract
2. Engineering Team
   1. UofA
   2. Contract
3. GMP Microlab
4. Current Personnel

Equipment

Current Operation

1. Current Personnel
2. GMP Microlab

New Operation

1. Commissioning Team
   1. UofA
   2. Contract
2. Engineering Team
   1. UofA
   2. Contract
3. GMP Microlab

Radiopharmaceutical Preparation

Current Operation

1. Current Personnel

New Operation

1. Current Personnel
2. Contract Validation Team

Quality Control and Documentation

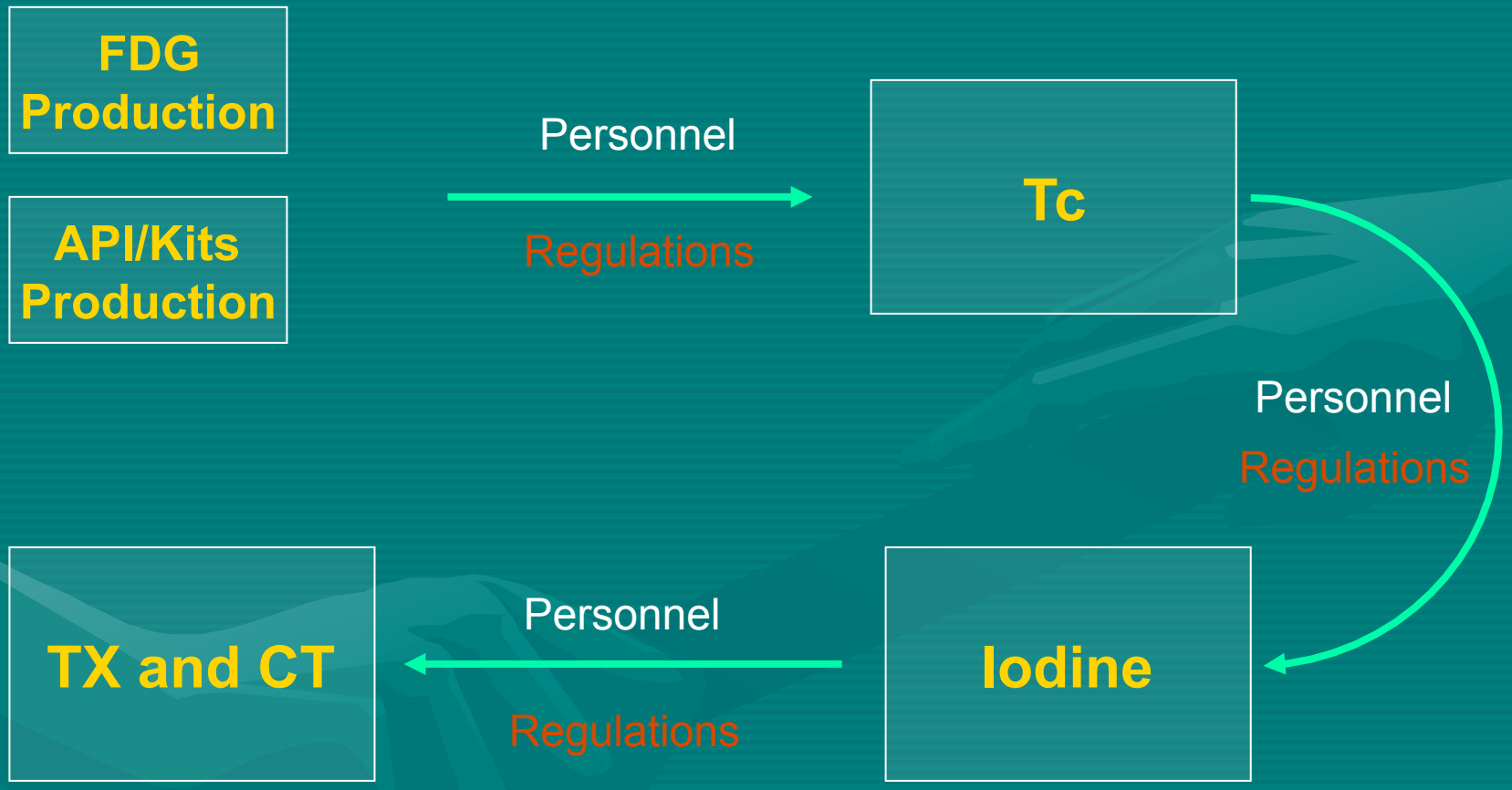
Current Operation

1. Current Personnel
2. 1 New QA Person

New Operation

1. Current Personnel
2. Contract Team

Phasing


FDG Production
API/Kits Production
Personnel
Regulations
Tc
Personnel
Regulations
Iodine
Personnel
Regulations
TX and CT

The End

FINISHED FILES ARE THE RESULT OF YEARS OF SCIENTIFIC STUDY

COMBINED WITH THE EXPERIENCE OF YEARS

There are 6 F's

The brain does not process "OF"

Score

3 is normal

4 is rare

5-6 is excellent