COLLABORATIVE THINKING BUILDS ROBUST QUALITY

Developing Combination Products

Donald Singer

AGENDA

- Combination Products
- Contamination Control
- Scope
- Responsibilities
- Resources and Valuable Information
- Focus on Quality Relationships

COMBINATION PRODUCTS

Under 21 CFR 3.2(e), a combination product includes:

1. A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity (such as a prefilled syringe or drug-eluting stent)
2. Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products (a “co-packaged” combination product)
3. A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved, individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed
4. Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect (another type of crosslabeled combination product).

COMBINATION PRODUCTS

In practice, (REALITY !)

Almost every sterile drug meets a delivery device when being administered to a patient.

Scope – A drug-device combination, e.g. pre-filled syringe with an autoinjector, containing a pharma or biopharma drug

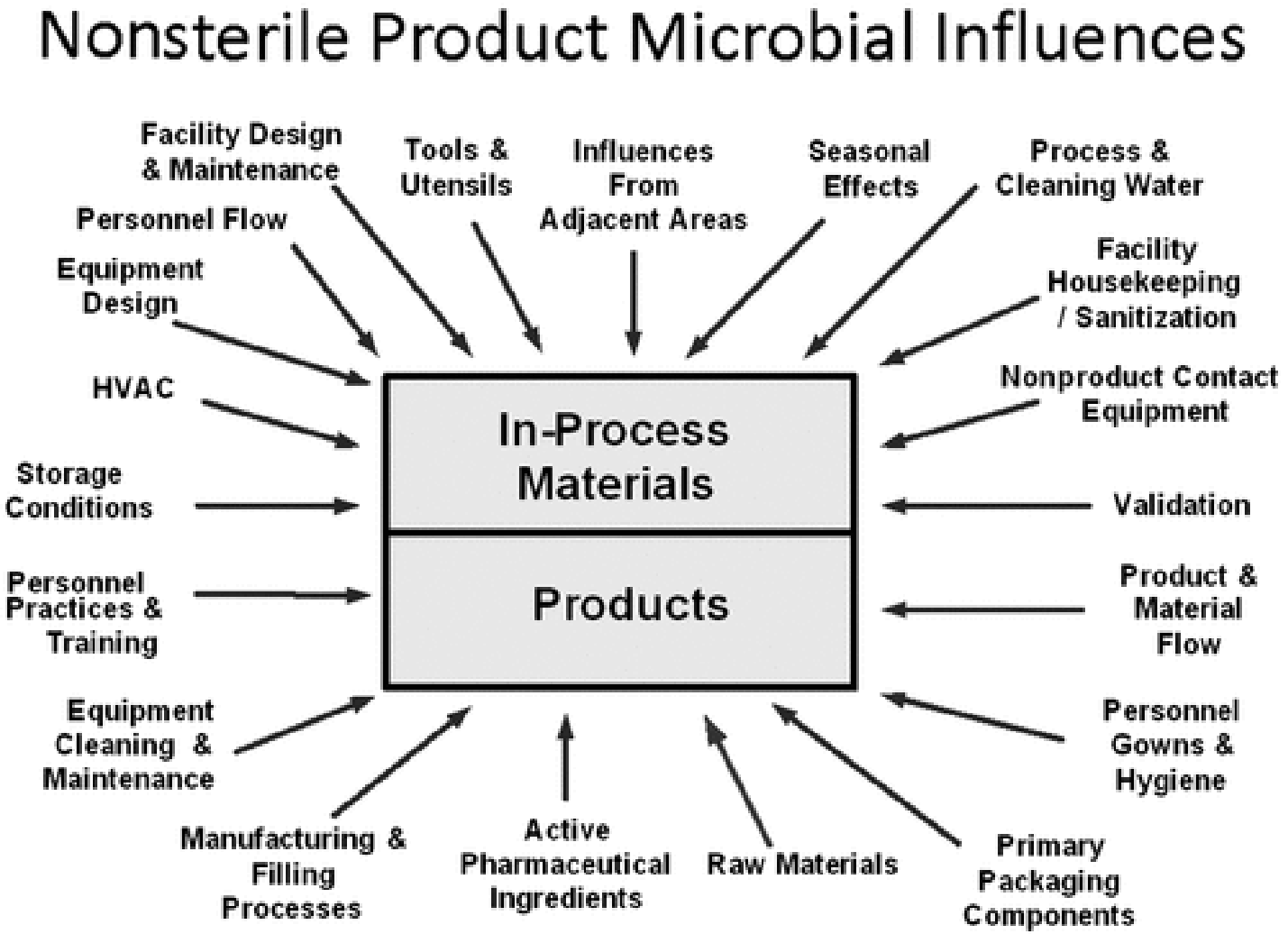
This is an R&D perspective for a new drug in development

CONTAMINATION CONTROL

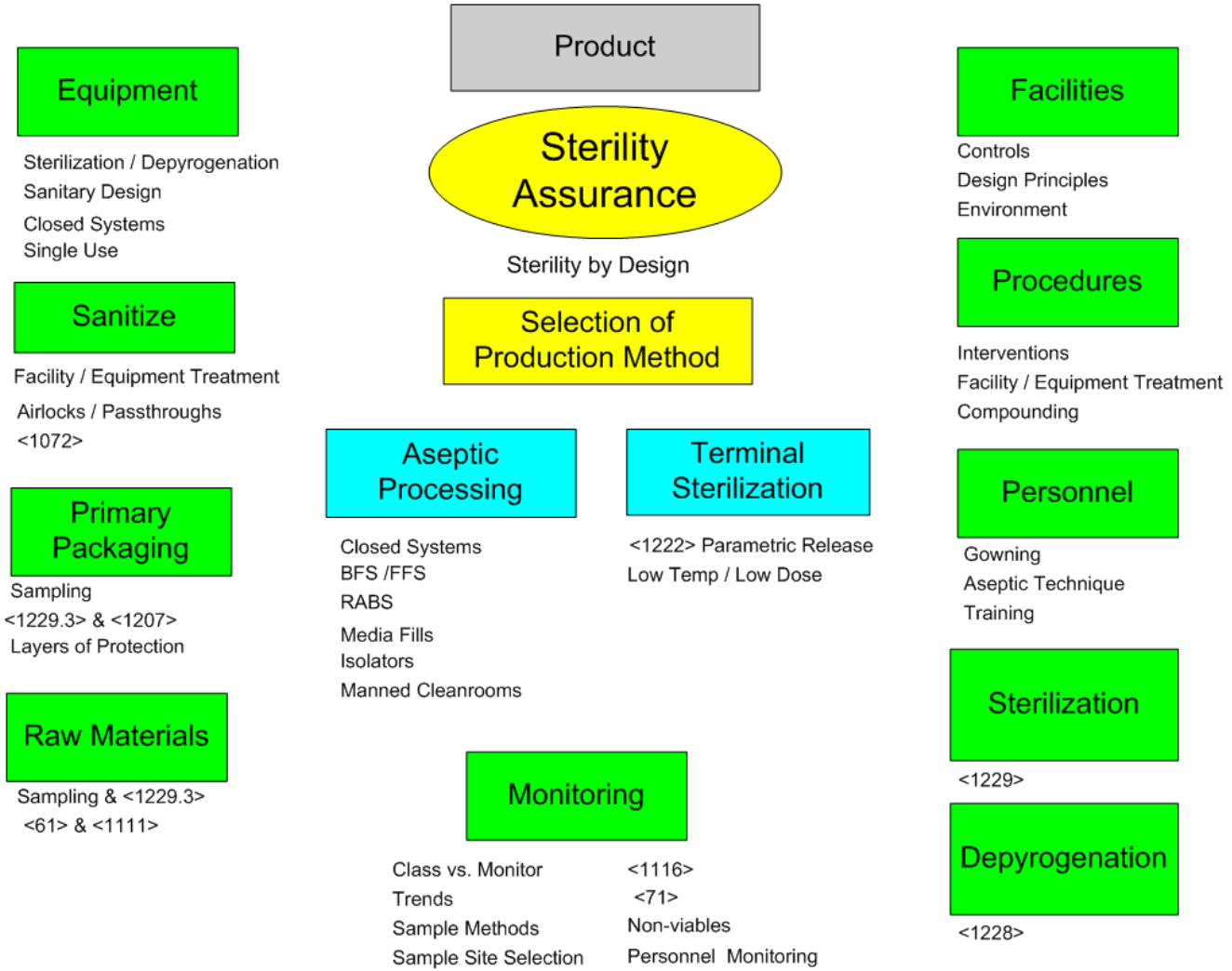
Six Sigma Approach

Risk Assessment for Quality

QUALITY CONTROL INPUTS – NON-STERILE



A STERILE PRODUCT PERSPECTIVE



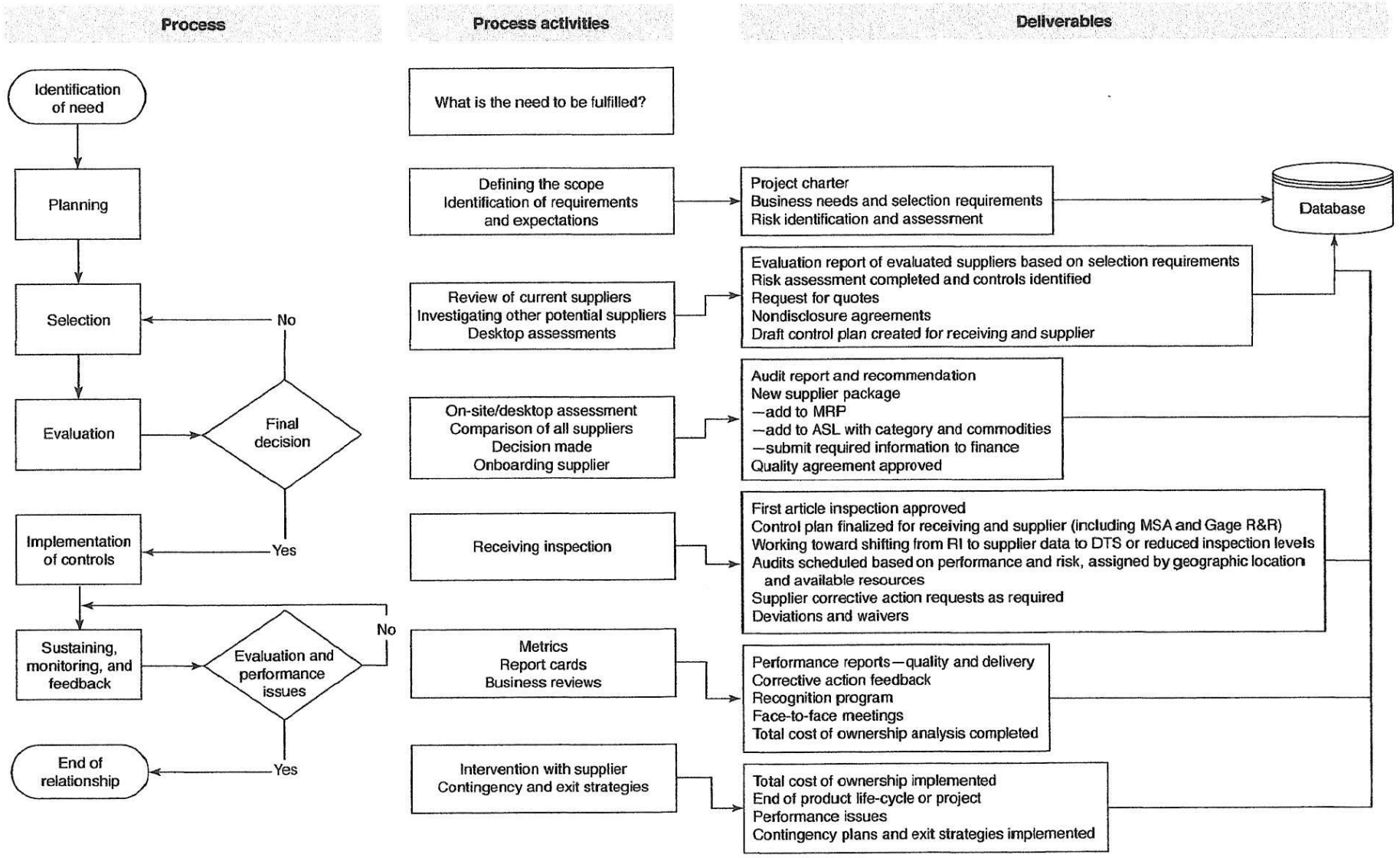
CONTAMINATION PREVENTION

Who has responsibility?

Drug developer – risk assessment of final product and device combination for patient use

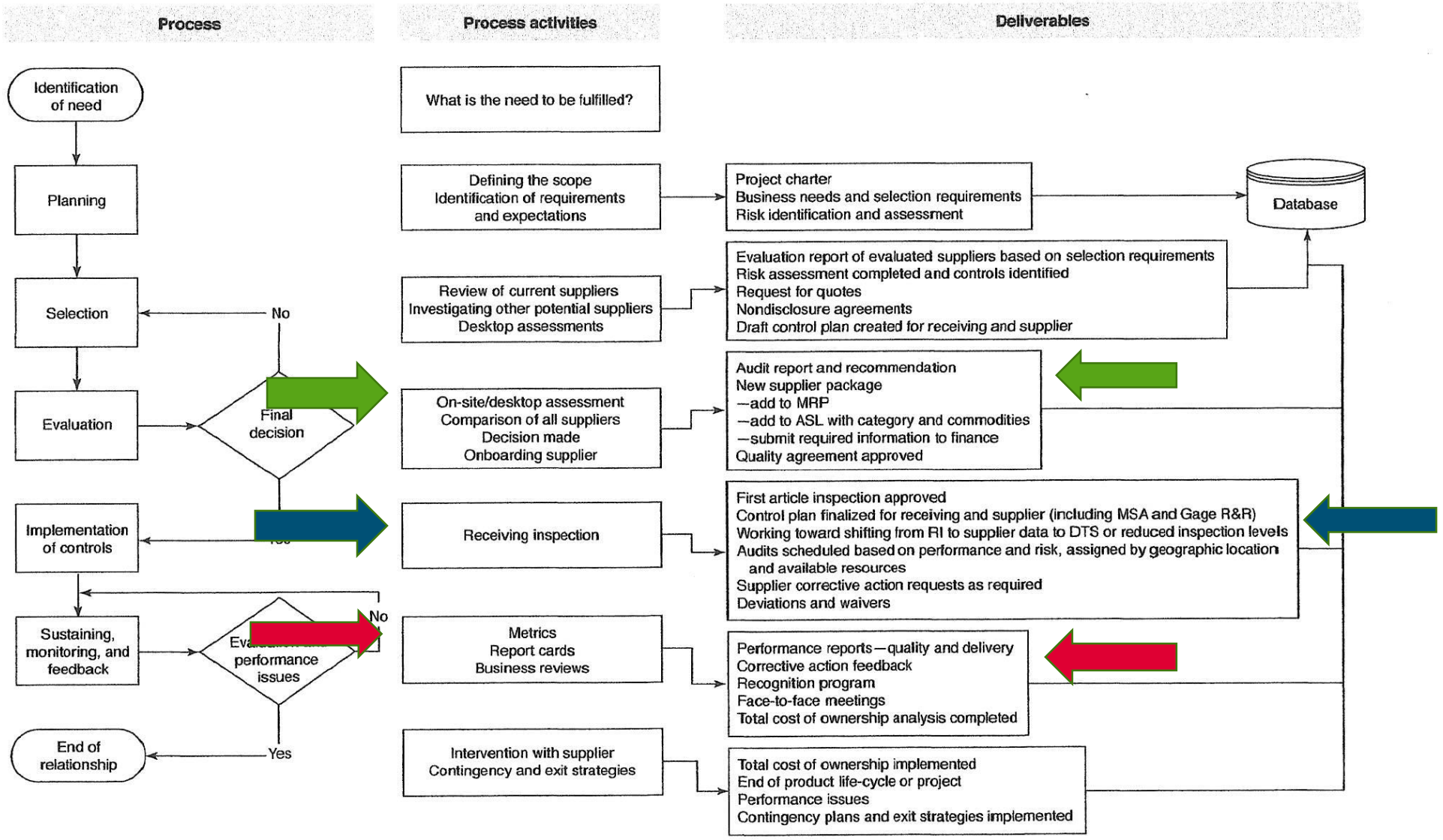
Device developer – risk assessment of life cycle of device through to patient use

ROAD MAP TO SUPPLIER MANAGEMENT



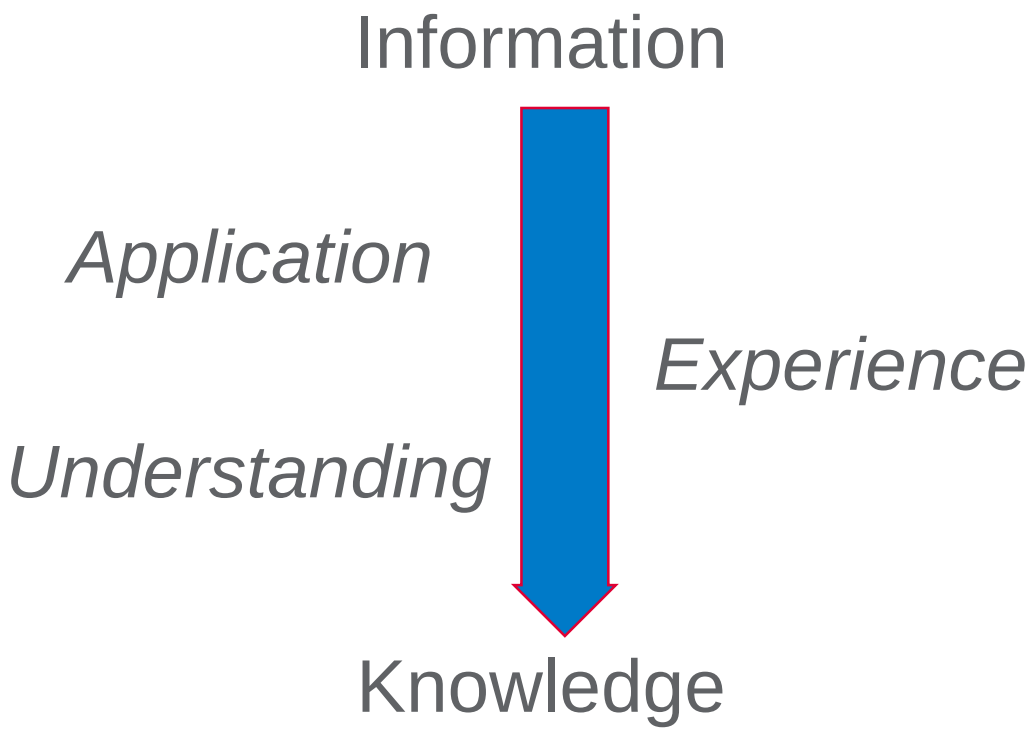
J. Shore and J. Freije, 2016

ROAD MAP TO SUPPLIER MANAGEMENT



J. Shore and J. Freije, 2016

VALUE OF CRITICAL INFORMATION



SOURCES OF CRITICAL INFORMATION

- Specifications
- Product registration information
- Process map
- Physician/clinician feedback or panel evaluation
- Clinical trials

WHAT IS RELEVANT TO MICROBIOLOGICAL CONTAMINATION CONTROL?

SPECIFICATIONS

Be able to evaluate and distinguish safety and purity from efficacy/performance

Drug specs: (impact, assess for device integrity or drug stability)

Device specs: (impact, assess for drug compatibility or patient safety)

REGISTRATION INFORMATION

Drug information: e.g. protein, or small molecule, or oligonucleotide, or liposomal, or somatic cell

Also consider form: liquid or lyophilized

Consider method of sterilization: terminal or aseptically filtered

Device information: method of sterilization of syringe, plunger/stopper, needle

FURTHER LEARNING

For device sterilization, if used for aseptic filling:

What is the method? Radiation (gamma or e-beam ?)

Parametrically released? Dosimetry?

Vmax development of max dose (or >25Kgy)?

Ethylene oxide?

Packaging, primary and possible secondary

How and when are parts assembled?

FURTHER LEARNING

Drug-device combination- Can it be terminally sterilized? What is the sterilization cycle development?

If moist heat sterilization used,

What is the time and temperature impact on the drug?

What is the time and temperature impact on the device?

Risk assessment is key to product registration and pre-approval inspection by the regulatory agency

PROCESS MAP

Device: RM supply → manufacture → storage → customer

Drug: RM supply → manufacture → storage (warehouse or clinic) → patient

Risk evaluation of each process will influence development of controls.

PROCESS MAP

Are all steps evaluated?

Is ‘assembly’ part of the manufacturing process or performed after the process?

(Key risk assessment often missed- assembly of auto/pen injectors)

Is container closure integrity (CCI) performed on filled combination product or with a surrogate?

Is CCI performed during stability?

PHYSICIAN/CLINICIAN INPUT

Device use panel or trial without drug

Actual clinical trial instructions assessment and practice runs

CLINICAL TRIAL

Factors to assess:

- Time of preparation and storage of prepared dose
- Handling of combination product during patient administration
- Specifics of handling if self-administered by patients compared to clinician administering

COLLABORATIVE THINKING IS NOT AN OPTION

Drug developers and Device developers need to communicate what is necessary to protect the patient!

Sharing knowledge is simple, but should be expected more

Using a quality systems approach including experts from both drug and device companies should occur before a combination product is evaluated by the regulators

THE PATIENT IS OUR ULTIMATE CUSTOMER

Combination products can be robust and safe for patients with adequate collaboration by the drug and device developers with a thorough quality and risk assessment approach.

Our customers depend on us to do it the right way!

Cleanrooms

Thank You!

ECOLAB®

Ecolab Life Sciences Complete Solution

Donald Singer
Donald.Singer@Ecolab.com

Clean In Place / Clean Out of Place

Vaporized Hydrogen Peroxide (Bioquell)