

The J&J Risk Based Exposure Assessment Process

IH & Containment Conference
Rome, May 14-16, 2013

Janssen Campus Belgium

Michel Vangeel

Principal Expert Industrial Hygiene & Ergonomics

mvangeel@its.jnj.com

ONE TEAM Making the Difference for Patients WORLDWIDE



Risk Based thinking

- **Risk** drives the decision, **hazard** is considered
- Prioritize activities, use of resources and future investments based on risk
- Risk Based thinking assumes that
 - Consider realistic scenarios
 - Integrates approach with QA, engineering and manufacturing
 - Relies on facts and data in the decision making process
- Without Risk Based Thinking
 - Infinite resources will be required to achieve objectives.

Where we were yesterday?

- Former J&J guidelines recommended containment specifications and controls based on OEL and Toxicity levels API.

Where we are Today?

- Recommends containment specifications and controls based on risk. Introduction of Risk Based Exposure Assessment Process (**RBEAP**) and Risk Based Exposure Assessment Control Guideline (**RBEAC**)

Risk Based Exposure Assessment Process (RBEAP)

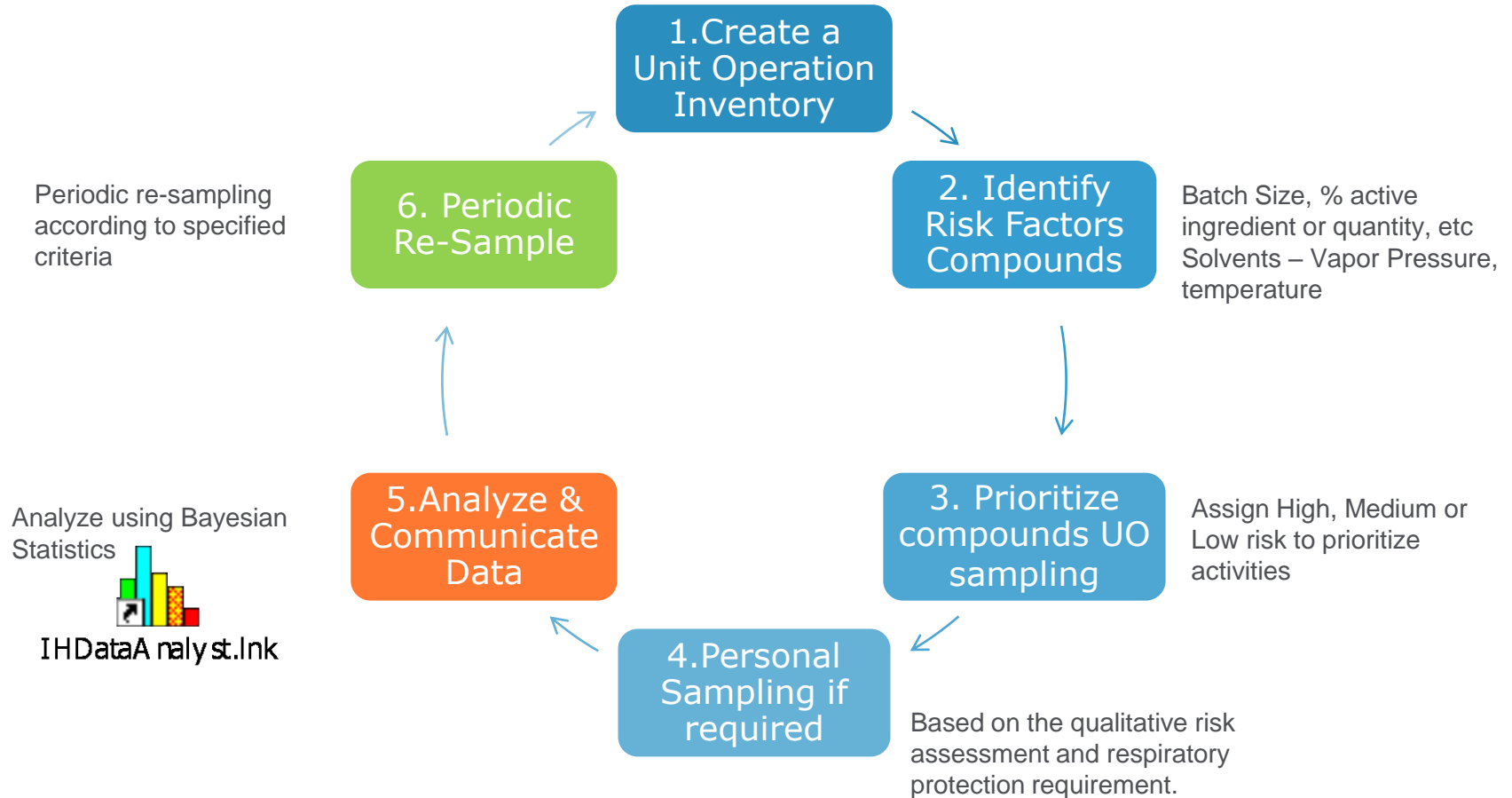
- Tool created by cross functional team, **IH Steering Team**
Janssen Supply Chain
- Process to systematically **assess** inhalation exposure **risks** of activities with Active, Pharmaceutical Ingredients and solvents
- Tool introduced step-by-step in Pharmaceutical Production, Chemical Production and R&D (training program, metrics)
- **Team Approach:** Use of stakeholders, involvement operations.

Risk Based Exposure Assessment Process (RBEAP)

- Provides a **lean**, systematic and pragmatic **methodology** to;
 - **Identify** the chemical **hazards** for each unit operation
 - Identify **priorities** for air **sampling** based on those products that have the potential to generate the highest airborne particulate concentration.
 - Organize the data so that **Similar Exposure Groups** can be established.
 - **Communicate** results to employees, medical and management using a transparent format.
 - Understand future IH air sampling needs and managing changes, ie impact of introducing new products.
 - RBEAP is used to **understand exposure risks** to be able to make **data driven decisions** to prioritize **containment projects**

Risk Based Exposure Assessment Process

Six Steps



Risk Based Exposure Assessment Process

Create inventory of Unit Operations

Powder Handling Unit											
Location	Unit Operations	SEG	Risk	Sampling complete reference last IH report	RBEAP date	APF1	APF2	APF3A	APF3B	APF4	Remarks
G120/221	API1 toevoegen uit container/müllerdrum zeefinstallatie PZE2	operator	H	IHG09-059	12.02.2010	50	50	1000	NA	NA	
G120/021	API2 aftappen in container/müllerdrum zeefinstallatie PZE2	operator	H	IHG09-059	12.02.2010	50	50	1000	NA	NA	
G120/021-221	API3 demonteren zeefinstallatie PZE2 voor reiniging	omsteller	H	IHG09-059	12.02.2010	50	50	1000	NA	NA	
G120/201	API4 toevoegen uit container/müllerdrum zeefinstallatie PZE3 - klein batch	operator	H	IHG08-088	12.02.2010	50	50	1000	1000	10000	
G120/019-219	API5 Aandocken cannisters SVA toren 1&2	operator	L	IHG09-017	12.02.2010	1	1	1	1	1	
G120/019	API6 aftappen zakjes - SVA toren 1&2	operator	L	IHG08-081	12.02.2010	1	1	1	1	1	
G120/217	API7 wisselen toevoegcontainer/müllerdrum maalmolen PMA1/PMZ1	operator	H	IHG09-056	11.02.2010	50	50	1000	NA	NA	
G120/017	API8 wisselen opvangcontainer/müllerdrum maalmolen PMA1/PMZ1	operator	H	IHG09-056	11.02.2010	50	50	1000	NA	NA	
G120/017	API9 controle maalmolenhuis PMA1/PMZ1	operator	H	IHG09-056	11.02.2010	1	50	50	NA	NA	
G120/017-217	API10 demonteren maalmolen PMA1 voor reiniging	omsteller	H	IHG09-056	11.02.2010	50	1000	1000	NA	NA	
G120/218	API11 wisselen toevoegcontainer/müllerdrum maalmolen PMA2	operator	H	IHG10-024	03.05.2010	50	50	50	NA	NA	
G120/218	API12 Toevoegen via zakkenstorttrechter PMA2	operator	H	IHG08-048	11.02.2010	50	1000	1000	NA	NA	

Document all information for each Unit Operation

General Information

Active compounds involved

Selection compound greatest potential airborne exposure

Respiratory protection required (based on analysis below)

Document results personal sampling

Analysis of the IH sample data for 'worst case' compound

Risk Based Exposure Assessment Process (RBEAP)											
Unit operation: Raw materials sampling and cleaning		Routine task (Y/N): Yes			Room - Name installation: E100 or 112		Date: 11/19/07				
Steps of unit operation/process: QA technicians collect samples by opening representative drums in lot and using a sample thief or scoop (from bottles in the case of Fentanyl) - they collect samples from the top, middle and bottom of the drum - samples are placed in glass jars that are sealed and delivered to the lab and retain area - drums are then closed and returned to vault area - local area is cleaned with IPA-wetted cloths											
Potential route of exposure: Inhalation and Dermal											
Section 1 - Follow-up/monitoring actions											
IH data isolator needed											
Photo								Exposure Control			
								Local exhaust should be positioned within 12" of sampling point			
Section 2 - API/product technical details											
API/Chemical	Product	PBCEL/OEL (ug/m3)	STEL Assigned (Y/N)	Particulate (u)	Dustiness (Y/N)	Solid Matrix (Y/N)	Batch Size(kg)	% of Active in Batch	Worst case (H,M,L) *	RPE Required? Type	APF required for RPE after interpretation data collected
Acetaminophen	PDP-6	1/3000 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	No respirator required based on data
Clonidine	Caspres	38/0.66 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Fentanyl Base	Duragesic	4/0.1 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Fentanyl HCl	lonays	4/0.1 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Hydrocodone Bitartrate	PDP-6	2/190 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 10 (based on statistics report 2307-017)
Hydromorphone HCl	AP-77	38/2 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Methylphenidate HCl	Concerta	2/40 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 10
Oxycodone Hydrochloride	Ditropan	2/40 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 10
Paliperidone	AP-E3	38/0.74 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Pseudoephedrine HCl	Sudafed	2/300 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	No respirator required based on data
Scopolamine Hydrobromide	Transderm SCOP	2/1 ug/m3 (OTR) (non J&J OEL)	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Verapamil HCl	Covera	2/160 ug/m3 (non J&J OEL)	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	No respirator required based on data
Section 3 - Air sampling results - personal											
API	Product	% API	Sampling Date	Sampling Time (min)	Worst Case (H,M,L)	Results (ug/m3)	Number IH report	Survey number OTE	Comments		
Hydrocodone HCL	AP-77	100	05/28/98	62	H	1.8	1998-008	52988	room E100A, sampled from 4 drums		
Hydromorphone HCL	AP-77	100	05/28/98	66	H	6	1998-008	52988	room E100A, observed operation, some assistance		
Hydrocodone HCL	AP-77	100	06/10/98	121	H	16	1998-008	52988	room E100A, sampled 8 lots		
Hydrocodone HCL	AP-77	100	06/10/98	104	H	1.5	1998-008	52988	room E100A, sampled source drums...		
Fentanyl Base	Transderm	100	04/02/97	97	H	1.2	1997-002	20497	room E100A		
Fentanyl Base	Transderm	100	04/02/97	97	H	7.5	1997-002	20497	room E100A		
Acetaminophen	PDP-6	100			H				No data available for this API		
Clonidine	Casapres	100			H				No data available for this API		
Fentanyl HCl	Duragesic	100			H				No data available for this API		
Hydrocodone Bitartrate	PDP-6	100	08/17/07	32	H	< 16	2007-017	NA	Not used for statistics below		
Hydrocodone Bitartrate	PDP-6	100	08/17/07	32	H	< 16	2007-017	NA	Not used for statistics below		
Hydrocodone Bitartrate	PDP-6	100	08/17/07	16 (STEL)	H	47	2007-017	NA	Not used for statistics below		
Hydrocodone Bitartrate	PDP-6	100	08/17/07	16 (STEL)	H	160	2007-017	NA	Not used for statistics below		
Methylphenidate HCL	Concerta	100			H				No data available for this API		
Oxycodone Hydrochloride	Ditropan	100			H				No data available for this API		
Paliperidone	AP-E3	100			H				No data available for this API		
Pseudoephedrine HCL	Sudafed	100			H				No data available for this API		
Scopolamine Hydrobromide	Transderm SCOP	100			H				No data available for this API		
Verapamil HCL	Covera	100			H				No data available for this API		
Section 4 - Summary of data											
Task Duration Vs. TWA	Number of samples	Mean (ug/m3)	Range (ug/m3)	Average Sampling Time (min)	Air Sampling Time Range (min)	95 percentile (ug/m3)	UTL 95, 95 (statistical analysis)	Conclusions			
Task Duration	6	5.6	1.2 - 16	94	62 - 124	20.4	1,77E+02	PPE chart: 99.6 % sure mask APF of 1000 is sufficient for Fentanyl (with OEL 0.1 ug/m3)			
TWA											
Section 5 - Unit operation risk ranking - (site customized)											

* Rationale: undependant of product sampled: similar exposure expected = all H

Risk Based Exposure Assessment Process

Conclusion



Former Approach

Not Risk Based.

Beyond Compliance

More resources and IH Costs.

(Need to sample for each API and process)

IH method required for every chemical

Sampling criteria were hazard based

Current Approach

Risk Based

Full regulatory compliance

Sampling criteria based on worst case scenario

Eliminates need to have IH method each API

Cost avoidance with resources and air sampling

Supports new product introduction, sourcing decisions and product transfers

Streamlining medical surveillance, All IH information in one document

Generates statistical data to drive risk based decisions investments

One format to share and communicate results (Internal + Ext)





Thank You

Janssen Campus Belgium

Michel Vangeel

ONE TEAM Making the Difference for Patients WORLDWIDE