PRACTICAL APPLICATION OF RISK ASSESSMENT IN PHARMACY PREPARATIONS BASED ON EUROPEAN RESOLUTION CM / RES AP (2011) 1

PP-013

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Background

The European Resolution CM/ResAP(2011)1, by affirming the importance of medicinal products prepared in pharmacy, says that before setting up a preparation, clinical needs of the patient should be evaluated in relation to the risk associated. The resolution states that it is necessary to adopt strict protocols of preparation to ensure the quality of the product, in addition to Pharmacopoeial requirements.

Purpose

To assign numerical risk value to each preparation in order to **assess** risk/benefit ratio and then to apply an adequate system of quality assurance.

Materials and methods

After the recent drafting by our National Society of Compounding Pharmacists (SIFAP) of a Position Paper on risk assessment, based on the Resolution, pharmacists and technicians of our hospital pharmacy collaborated to classify preparations as low, medium-low, medium-high and high risk, by assigning the values, as tabulated in the document, for pharmacological risk, preparation process risk, risk depending on number of preparation per year. By entering the values obtained and using a defined formula by specific excel worksheet we calculated the overall **risk value (VR).**

VR = X + (Y x Z)

X = Pharmacological risk

High Risk AI*: low TI*, cytotoxic AI, i.v. route of administration >>>> **125**
High Risk AI*: low TI*, cytotoxic AI, all route of administration except i.v. >>>> **120**
Medium-High Risk AI*: acute toxicity rank 1 or 2 and Table 3 FU Italian XII ed. >>>> **75**
Medium Risk AI*: i.v. route of administration >>>> **50**
Medium Risk AI*: all route of administration except i.v >>>> **25**
Low Risk AI*: AI* without specific toxicity >>>> **1**

***Active Ingredient**
***Therapeutic Index**

Y = Preparation process risk

Criteria \ Score	1	2	3	4	5
A. Calculations	Max 5 operations	-	Over 5 operations	-	Isotonic calculation and preparation check
B. Weighting operations, powders dilution, liquids addition	Max 3 operations	-	More than 3 operations or amount less than 5 ml	-	More than 6 operations
C. Uniformity of dosage	Solutions, semisolid preparations	Suspensions	Solids (capsules, powders, suppositors, ovules...)	Tablets	Monodose Dosage forms less than 2mg or multidose dosage forms less than 0,01 %
D. Type of preparation	Cutaneous and transdermal preparations	-	Preparations for gastroenteric tract	Sterile preparations for cutaneous and transdermal use, Preparations for gastroenteric tract , inhalation and ophtalmic use	Sterile preparations, ophtalmic preparations
E. Numbers and type of operations	Max 2 substances (excipients included) or only weighting and subdivision	3 substances or more than 3 manipulations or weighting, mixing and subdivision	3 substances or more than 4 manipulations or only one heat process	3 substances or more than 5 manipulations or operations that require specific methods or one filtration process	More than 3 substances or more than 6 manipulations or sterile process

Z = Risk related to number of preparation per year

Under 10 preparations >>>> **0,2**
From 10 to 100 preparations >>>> **0,8**
From 100 to 500 preparations >>>> **1**
Over 500 preparations >>>> **1,5**

Results

Ten preparations, (non-sterile, sterile, oncology IV, intrathecal, TPN), have been analyzed and classified using this method, resulting in different values. It was also noted that different formulations, with the same active molecule and therapeutic use, can generate different values. E.g., spironolactone obtained a value of 34.6 (low risk) as oral suspension versus 325 (high risk) as unit-dose oral powder. This instrument can be used to support the choice between different options of formulation, as well as a stimulus for development and improvement of quality, safety and effectiveness of drugs prepared in pharmacy.

RISK ASSESSMENT	
SPIRONOLACTONE UNIT-DOSE ORAL POWDER	
Pharmacological Risk (X)	25
Preparation process risk (Y)	-
A	1
B	5
C	5
D	3
E	5
TOT	375
Risk related to number of preparation per year	0,8
RISK VALUE	325

VS

RISK ASSESSMENT	
SPIRONOLACTONE ORAL SUSPENSION 2,5MG/ML	
Pharmacological Risk (X)	25
Preparation process risk (Y)	-
A	1
B	1
C	2
D	3
E	2
TOT	12
Risk related to number of preparation per year	0,8
RISK VALUE	34,6

VR	Risk Index	Quality System
Max 50	LOW	Working area not separated or not separable (or NBP*)
51 < VR ≤ 100	MEDIUM-LOW	Working area separated or separable (or NBP*)
101 < VR ≤ 225	MEDIUM-HIGH	Complete NBP*/ Periodic Quality controls on the method
> 226	HIGH	Complete NBP*/Scheduled(time planning) quality control on the method and preparation

Good Compounding Practice - GCP

Conclusions

The method of risk assessment proposed is very useful for the activities performed in our laboratory; however, there are some aspects which require further reflection, such as how much computerization and automation of processes or specialization of operators, related to the annual amount of products prepared, affect the overall risk value related to pharmacy preparations.

Type of preparation	VR
Gel support	6
Eyedrops	50
Pancrelipase Capsules	70
Bosentan Oral Suspension	101,2
Spinal Tap	200
Fotemustine iv bag	200
Rituximab iv bag	237,5
Total parenteral nutrition bags	1062,5

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