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## **Risk attitudes and personality traits predict perceptions of benefits and risks for medicinal products: a field study of European medical assessors**

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## Abstract

**Title: RISK ATTITUDE AND PERSONALITY TRAITS PREDICT PERCEPTIONS OF BENEFITS AND RISKS FOR MEDICINAL PRODUCTS: A FIELD STUDY OF EUROPEAN MEDICAL ASSESSORS**

Risk attitudes and personality traits are known predictors of decision making among laypersons but very little is known of their influence among experts participating in organizational decision making. Seventy-five European medical assessors were assessed in a field study using the Domain Specific Risk Taking scale (DOSPERT) and the Big Five Inventory scale. Assessors rated the risks and benefits for a mock 'clinical dossier' specific to their area of expertise and ordinal regression models were used to assess the odds of risk attitude or personality traits in predicting either the benefit or the risk ratings. An increase in conscientiousness score predicted an increase in the perception of the drug's benefit and male assessors gave higher scores for the drug's benefit ratings than female assessors. Extraverted assessors saw fewer risks and assessors with a perceived neutral-averse or aversive risk profile saw greater risks.

Word count: 141

**Key Words: Risk attitude, Personality, Benefit-Risk, Individual Characteristics, Risk Perception, Benefit Perception**

## **Introduction**

Regulation of medicinal products in Europe is conducted within a complex organizational structure encompassing over 40 National Competent Authorities (NCA) and relying on the expertise of 4,500 experts or medical assessors throughout the EU (1). A substantial part of the assessment is under the responsibility of the medical assessors who work individually, or within groups, in the NCAs to evaluate the benefits and the risks of medicinal drugs. In the field of risk research, there are several well established findings that may be relevant to decision making for the regulation of medicines: (1) that benefit perception is the inverse of risk perception (2); that the personality taxonomy from the Big Five Inventory may intersect with risk attitudes and explain differences in risk taking (3); and that risk attitudes (risk seeking, risk neutral, risk averse) are important descriptors for the shape of a decision maker's utility function underlying his/her choices (4-6). A full discussion of each of the above mentioned findings are beyond the scope of this manuscript; however a brief summary of the literature and references to more detailed publications is provided below.

Alhakami and Slovic have observed that laypersons have a negative correlation between benefits and risks in that an activity or technology judged high in benefit is judged low in risk and vice versa(2). An inverse relationship between benefit and risk perception implies the use of a heuristic, a subconscious rule of thumb that simplifies decision making by considering only a subset of the available information when arriving at a decision. The work of Gigerenzer and Brighton (2009) and others support the view of heuristics as an efficient means for managing uncertainty as it minimizes the need for complex computations when assessing situations and in many cases allows one to arrive at a similar level of accuracy as logic-laden decisions (7-9). There may however be instances where the application of a rule of thumb or a heuristic such as benefit high/ risk low may be inappropriate given that medicines can have both increased

benefits and increased risks. Therefore evidence of the use of such a heuristic among assessors could indicate the introduction of biases in the decision making for medicinal drugs. It is therefore of interest to show if this benefit/risk heuristic operates among assessors as it does for laypersons or if there other important predictors of benefit-risk perception. Personality traits are known indicators of risk taking in that persons with higher levels of the traits extraversion and openness to experience tend to increase risk taking while conscientiousness, neuroticism and agreeableness decrease risk taking (8, 10). Very relevant for organizational performance, these traits have also been found to predict creativity and generation of superior ideas when an 'optimal' balance of personality traits is achieved within working teams (11). Risk attitudes, when translated into the drug regulatory context, could imply that an assessor who is risk averse may be willing to give up the benefit a drug could provide to avoid the uncertainty regarding long term side effects, while a risk seeking assessor may be willing to accept some risks to avoid the sure loss of the drug not reaching the market. A risk neutral/tolerant assessor may be seen as having an impartial view with a willingness to accept some degree of risk in every situation (4, 12). The risk attitude that is most often assigned to medical regulators is one of risk aversion (13, 14); however there is no concrete evidence that medical regulators are uniformly risk averse. Despite its appeal, the term 'risk attitude' as a stable individual trait (e.g., a person who exhibits a risk averse utility function *does not like to take risks*), has had limited empirical support (6, 15, 16). Work from Weber and others have shown that individuals are not stable in their attitudes towards risk and may shift from being risk neutral to risk seeking depending on the domain (e.g., health versus finance (15, 17). However, Weber's research has also shown that an individual's perception of the riskiness of a situation may be the lever that shifts risk attitude from averse to

seeking, therefore identification of a stable perception, if such exists, may be of great value in understanding individual or group decisions under situations of risk.

The above mentioned research has been predominantly carried out among laypersons; experts have rarely been included in these studies primarily due to the assumption that given their expertise they consider only objective data when making judgments of risk and are not influenced by other factors (18, 19). There is growing evidence to contradict this view and the authors direct the readers to the work of Sjoberg and others (20-23). In 2009, the European Medicines Agency (EMA), the central body for regulating medicines in Europe, launched the EMA Benefit-Risk Methodology Project to assess the applicability of decision support tools within the regulatory environment. (24-26). Medical assessors in five European countries participated in field tests of methods aimed at improving the transparency of decision making (27, 28). One case study, not originally planned at the onset of the project, was the market authorization of the H1N1 (Swine Flu) vaccine. At the time, there was a genuine public health concern regarding the global impact of an impending contagious and sometimes fatal disease, and a decision regarding the market authorisation of the vaccine was urgently needed. This, coupled with the lack of data on the efficacy and safety of the vaccine, created a highly charged environment. Consistent with the objectives of the EMA BR project, senior administrators at the EMA undertook to participate in a multi-criteria decision analysis (MCDA) workshop (external to the normal decision making process) to clarify their individual attitudes towards the benefits and risks of early or late approval of the vaccine. The result was a decision model that increased transparency of the assumptions regarding the number of expected fatalities if the decision was advanced or postponed. While the final decision was not taken during this process the use of this methodology aided in defusing the tensions surrounding the decision by highlighting differences

in risk attitudes among the participants and facilitating a more structure discussion of the implications to approve or not approve the vaccine (29).

Not all regulatory decisions are as charged as that of the Swine Flu vaccine, that is, a heightened emotional situation due to the potential for global fatalities with limited available data and short time period within which to consider the decision; but this is not the only situation in which it may be appropriate to apply tools that support the regulatory process and remove the potential for introduction of biases in the decision making. If regulatory experts, like laypersons, are influenced by factors external to the scientific data even when working within their area of expertise, then tools like MCDA or other structured approaches to decision making should be employed by medical assessors to support their work. In this study, we aim to examine the risks and benefits of medicinal drugs as perceived by expert regulators, and to assess the influence of personality traits and risk attitudes on their perceptions. Treating Weber's risk attitudes across domains as a measure of stable risk attitudes, our hypothesis is that assessors use the heuristic--benefit perception is the inverse of risk perception-- and personality traits and risk attitudes that indicate greater risk taking among laypersons will also be found to indicate greater risk taking among assessors. The objectives of this study are therefore: (1) to describe the distribution of risk attitudes among medical assessors; (2) to measure their personality traits and cross-domain risk attitudes; (3) to measure the correlation between benefit rating and risk ratings of a medicinal product; (4) to predict the benefit and risk ratings of a medicinal product using the measured personality traits and risk attitudes.

## **Methods**

The study was implemented as a web-based questionnaire and launched between June 2010 and October 2010. Medical assessors from nine European National Competent Authorities (NCAs)

were identified by their agency and invited to participate. Demographic data were collected covering gender, country, age, education level, years in regulatory role, clinical area of expertise (clinical efficacy, clinical safety, non-clinical), and therapeutic area of expertise: Central Nervous System (CNS), Cardio-vascular and Oncology. Data were collected in three phases with each phase lasting approximately six weeks: Phase 1: Demographic data, Domain Specific Risk Taking scale (DOSPERT)(30); Phase 2: Drug Case Study using a mock 'clinical dossier'; Phase 3: The Big Five Jackson Inventory personality test(3).

### Domain Specific Risk Taking Scale

A number of scales have been developed to capture risk attitudes or behaviour but the DOSPERT was found to be most appropriate to the aims of this study as it captures attitudes towards risk taking within several defined domains (social, financial, health/safety, recreational, and ethical) that encompass general life situations. In addition, the DOSPERT scale captures not only the attitude towards several types of activities but also the measurement of an individual's perception of the riskiness and the benefits of that activity.

The description of the DOSPERT scale provided by the authors is as follows: The *risk-taking* responses of the 30-item version of the DOSPERT scale evaluates behavioural intentions -or the likelihood with which respondents might engage in risky activities- originating from five domains of life (i.e., ethical, financial, health/safety, social, and recreational risks), using a 7-point rating scale ranging from 1 (*Extremely Unlikely*) to 7 (*Extremely Likely*). Sample items include "Having an affair with a married man/woman" (*Ethical*), "Investing 10% of your annual income in a new business venture" (*Financial*), "Engaging in unprotected sex" (*Health/Safety*), "Disagreeing with an authority figure on a major issue" (*Social*), and "Taking a weekend sky-diving class" (*Recreational*). The *risk-perception* and the *benefit-perception* scales poses the

same questions as found in the risk taking scale but here the aim is to evaluate the respondents' assessment of the riskiness or the benefits of each activity, using a 7-point rating scale ranging from 1 (*Not at all risky*) to 7 (*Extremely Risky*)(17) and 1 (*Not at all beneficial*) to 7 (*Extremely Beneficial*) . Only the risk taking and risk perception scales of the DOSPERT were included in the current study. The addition of the benefit perception scale was felt to be too burdensome for the assessors given the length of the questionnaire. In addition, the benefit perception scale and the risk taking scale of the DOSPERT may be highly correlated as willingness to engage in an activity may be dependent on the benefit one perceives in that activity.

The scores of the risk taking and risk perception scales were added across all items of a given domain subscale to obtain risk taking scores. Higher scores suggest a propensity for greater risk taking in that domain. Similarly for the risk perception scale, item ratings are added across all items of the domain subscale to obtain risk perception scores and higher scores indicate a greater perception of risk.

Risk attitudes for both the risk taking and risk perception scales are presented in two ways as previously reported by Weber and others(31); by domain and across the domains. The authors believe that both presentations are justified in that Weber has proposed that a given risk attitude may be reflected within a specific domain but the measurement across all domains will reflect the general risk attitude of a person irrespective of domain. For each domain, respondent scores for both the risk-taking and risk perception scales were categorized as risk seeking, risk neutral and risk averse. Assessors whose sub-scale score was 1 standard deviation above or below the mean were categorized as risk seeking or risk averse respectively; otherwise they were categorized as risk neutral. For the analyses across domains, two new descriptors were used to categorize risk attitudes, reflecting the risk taking scale and the risk perception scale: general risk

attitude (GRA), and perceived risk attitude (PRA). Across the domains, the risk attitude of each assessor was classified as either seeking, seeking/neutral, neutral, neutral/averse, averse, or mixed depending on her/his risk attitude found previously within each of the domains. An assessor's general risk attitude was categorized as seeking if he/she was identified as risk seeking for all five domains on the risk taking scale. If the assessor was classified as seeking for up to 3 domains and then neutral for the remaining, they were categorized as seeking/neutral. Similarly, the perceived risk attitude was categorized as perceived neutral if the assessor was neutral for all five domains on the risk perception scale. In cases where the assessors moved from risk seeking to neutral, the assessors were categorised as perceived seeking/neutral. The 'mixed' category identifies those who had no discernible pattern in their risk attitudes, e.g., for one domain they were seeking, another averse, and for another domain neutral.

Statistical analyses of the correlation between the benefit rating and the risk rating and also the mean risk taking score and the mean risk perception score by domain were assessed. Statistically significant Spearman correlation coefficients were set a priori at  $<0.05$ .

### Mock clinical dossiers

In the second phase of the study, assessors were given a mock 'dossier' depending on their therapeutic area of expertise (Cardio, CNS, and Oncology). The cardiology product was indicated for treatment of atrial fibrillation; the oncology product was indicated for the treatment of non-small cell lung cancer; and the CNS product was indicated for the treatment of neuropathic pain. Data for the mock dossiers were adapted from the original product dossiers, Day 80 assessment reports and European Public Assessment Reports (EPARs)(32). The result was a shortened version of a real dossier with product-identifying data (e.g., drug name, manufacturer and dates) removed or substituted. The assessors were asked to review the dossier

and to give their perceptions by rating the medicinal product on two dimensions, risk and benefit. Both ratings used a Likert-like scale from 1-7; for the risk dimension the question was ‘How risky is this product?’ Possible risk ratings ranged from 1= *not at all risky* to 7= *extremely risky*. For the benefit dimension the question was ‘How beneficial is this product?’ Benefit ratings ranged from 1= *not at all beneficial* to 7= *extremely beneficial*. The assessors were constrained not to consult with their colleagues as the aim of the study was to collect their individual benefit and risk perceptions of the medicinal products.

### *Big Five Inventory (BFI)*

Five domains of personality (Extraversion, Openness, Neuroticism, Conscientiousness, and Agreeableness) have been consistently identified using various instruments over several decades and across many cultures and is therefore a highly regarded taxonomy (33-35). The Big Five Inventory scale that has been used in this area of research is a self-reported 44-item questionnaire to which respondents are asked to indicate if they strongly agree, disagree, are neutral, agree or strongly agree. An example of the description for openness would include ‘*I have a rich vocabulary*’, ‘*I have a vivid imagination*’, ‘*I have excellent ideas*’ (3, 36). Mean scores and standard deviations for each trait are presented. Higher scores within the domains indicate a greater propensity for the personality trait being measured.

### *Model Building*

Ordinal regression models were used to evaluate the relationship between the rating of benefits and risks for a medicinal product (one product in each of the disease areas previously mentioned) BFI traits and the risk attitudes from the DOSPERT scale. Ordinal regression models are an extension of the general linear model to ordinal categorical data. This method is very useful in

social sciences where data are often captured as ordinal variables limiting the usefulness of linear models that require interval variables. The ordinal model tests the probability of any category of the independent variables being in a particular category of the dependent variable or lower, compared to a reference group. Negative parameter estimates indicate lower scores for the benefit or risk ratings while positive estimates indicate choosing higher scores. For both the general risk attitude (GRA) and perceived risk attitude (PRA) the category with the largest proportion of assessors was the seeking-neutral group and this was therefore chosen as the reference category.

Due to limited published data on personality traits and experts, several models were evaluated responding to our research objectives. In order to determine which of the BFI dimensions was most relevant to this analysis, bivariate analyses were conducted using a backwards stepwise regression selection procedure between benefit as well as the risk ratings and the five dimensions of the BFI. At each iteration of the model, the BFI dimension with the lowest non-statistically significant Wald statistic was dropped. Assessors reviewed dossiers relevant to their area of expertise therefore a variable, denoting the three medicinal products in the mock dossiers, was included during model building. In previous research, gender has been found to be predictive of risk perception and so was also included in the models. Previous work in this area has shown a correlation between willingness to engage in risky activities depending on how risky the activity is perceived therefore separate models evaluating GRA and PRA were built.

Following the bivariate analysis described above, separate models were built for the benefit ratings and the risk ratings. The benefit ratings were regressed on the BFI personality traits identified from the bivariate analysis along with the GRA categories, gender, and therapeutic area. A forward and backwards stepwise regression selection method was used to determine the

final model with the best model fit(37). Variables with non-statistically significant estimates ( $>0.05$ ) were removed at each iteration. The evaluation of the benefit ratings and the PRA categories, gender and therapeutic area followed the same model building approach as above. This process was replicated for building the models for the risk ratings. All parameter estimates with statistically significant results at the  $<0.05$  level are reported along with data for model fit. The authors are aware that the use of stepwise regression methods have several limitations and that there are alternatives to this approach (e.g., testing the final model in an independent sample) but given the peculiarity of the study sample i.e., the limited availability of European medical assessors, the uniqueness of the sample population and the number of variables included for testing (DOSPERT, Big Five taxonomy) the chosen approach appeared to be the most pragmatic. All statistical analyses were conducted using SPSS 18.

## **Results**

### *Demographics*

Of the 80 assessors enrolled in the study, seventy-five (94%) responded in Phase 1, while fifty-nine (73%) assessors completed phases 2 and 3. No difference was found for age, gender, role in the agency, regulatory experience or therapeutic area expertise between the dropouts from Phase 1 and those who continued on to Phase 2 and 3.

As shown in **Table 1**, the group was equally balanced by gender; 31% was between 20 and 39 years old. Many assessors have multiple degrees; counting the highest degree attained, 51% of the assessors were medically qualified (51%) followed by PhD (29%) and pharmacists (13%).

Assessors within the NCAs generally focus on one area of expertise. In our sample the majority

of the assessors were experts in assessing clinical efficacy (63.8%). Assessors with more than 5 years of experience comprised the majority of the group (45%).

### *Risk Attitudes among Assessors*

The mean scores for the DOSPERT scales (risk taking and risk perceptions) for the five domains (social, financial, health/safety, recreational, and ethical) are shown in [Table 2](#). When the domain subscale scores for both risk taking and risk perception scales were categorized by domain, assessors were predominantly risk neutral/tolerant with the remaining assessors evenly distributed among the other categories ([Table 3](#)). When the risk taking scale was evaluated across the domains as shown in [Table 4](#), 2.5% of assessors were risk seeking for all domains, no assessor was risk averse for all domains and 15% of assessors were neutral/tolerant in their general risk attitude. Similarly for the risk perception scale, 2.5% of assessors were categorized as being ‘perceived risk seeking’ for all domains and 2.5% were ‘perceived risk averse’ for all domains, while 17.5 % of assessors were perceived risk neutral/tolerant.

As previously stated earlier research has shown a relationship between willingness to engage in risky activities depending on how risky the activity is perceived. We evaluated this using a correlation analysis between risk taking in each domain and the corresponding risk perception of the activity. There was a statistically significant inverse relationship between mean risk taking score and mean risk perception score ([Table 5](#)) for all domains with the exception of the social domain. The correlation analysis shows that the riskier an activity is viewed by the assessors, the less likely they are to engage in it.

### *Big Five Inventory*

The scores for the BFI dimensions were normally distributed with the following mean scores and standard deviations: Extraversion 3.3 [.738]; Conscientiousness 4.1 [.627]; Agreeableness 3.8 [.443]; Neuroticism 2.5[.704]; Openness 3.9[.461]. The regression coefficient of the bivariate analysis for the BFI dimensions showed only Conscientiousness (BFIC) to be predictive of the benefit rating (.519;  $p=.027$ ), that is, more conscientious individuals saw more benefit.

Extraversion (BFIE) was found to be predictive of the risk rating (-.406;  $p=.047$ ), such that the more extraverted assessors saw less risks attached to the drug. All other BFI dimensions were non-significant and therefore excluded from further modelling.

#### *Distribution and correlation of the Benefit and Risk Ratings*

For both the benefit and risk scales the ratings have a normal distribution with the majority of the ratings in the middle of the 1-7 range. The ratings were reclassified from ordinal to interval variables for the purpose of the correlation analysis and a statistically significant inverse correlation between the benefit and risk ratings was found (-.309;  $p=.017$ ).

#### *Ordinal Regression for the Benefit Rating – General Risk Attitude, Perceived Risk Attitude and BFIC*

It has been shown above that BFIC (conscientiousness) was predictive of the benefit ratings; the addition of the GRA categories did not improve the model and was therefore dropped. Gender differences have been found in many studies in risk taking and males in general have been found to be more risk taking and to perceive fewer risks than females (38, 39). Gender and therapeutic area were added to the model but therapeutic area was not statistically significant and did not improve the model fit and was therefore removed. With only BFIC and gender in the model the PRA categories were added but as with the GRA categories this variable was not statistically

significant. The final model was therefore BFIC (.497;  $p=.036$ ) and gender (.594;  $p=.041$ ) showing that controlling for gender, an increase in the score for conscientiousness increased the probability of giving higher benefit scores and similarly controlling for BFIC, male assessors gave higher benefit scores than female assessors [Table 6](#).

### *Ordinal Regression for the Risk Rating – General Risk Attitude, Perceived Risk Attitude and BFIE*

As above, the starting point for the model structure was the bivariate analysis with the risk ratings and BFIE (extraversion). Additional bivariate models for GRA (Chi-Sq 1.267;  $p=.867$ ), gender (Chi-Sq .206;  $p=.650$ ) and therapeutic area were constructed and all were shown to be non-predictive of the risk ratings with the exception of the therapeutic area [Table 7](#). Using the model with therapeutic area as the basic model the other predictor variables of interest were again added or dropped depending on whether an improvement in the model fit was observed. BFIE and the PRA categories along with therapeutic area resulted in the most robust model for predicting the risk ratings [Table 8](#). Assessors with higher scores for extraversion were more likely to give lower risk ratings. Compared to those in the perceived risk seeking-neutral category, the neutral-averse, aversive and mixed categories were more likely to give higher risk ratings, controlling for therapeutic area.

## **Discussion**

To our knowledge this is the first study to examine personality traits and risk attitudes within the pharmaceutical regulatory network in Europe and to study the relationship between risk perception and benefit perception among expert assessors, as measured by the benefit and risk rating of the medicinal products. One of our key findings is that, as for laypersons, benefits and

risks are inversely correlated among medical assessors. We believe that this is indicative of a heuristic which may in some cases be veridical, that is, truly reflective of the assessment of the drug but may also lead assessors to negate true benefits where there are high risks and prevent a balanced assessment. This inverse relationship of benefits and risks, while providing us with an important view of the mental model of experts in drug regulation should not serve as the sole explanation of the assessment process. We argue, based on the results of this study that the mental models of assessors are far more complex than previously assumed and that assessors rely on a complex interplay of risk attitudes and personality traits as well as the perception of the clinical data when assessing medicinal drugs.

The results from the DOSPERT scale are useful in countering a pervasive view that regulators have a shared and stable 'risk averse' attitude(13, 14, 40). Instead we show that for the domains measured, assessors are predominantly risk neutral/tolerant and may even perceive fewer risks than the sample of US undergraduates in the Weber et al. 2002 study (17). With the exception of risk neutral attitude, there was no evidence of assessors having a predominant risk attitude, i.e., risk seeking or risk averse across all domains; in line with previous research among laypersons, assessors change their risk attitude, e.g., move from seeking to neutral, or neutral to averse depending on the domain. However, it may be that within the risk attitude categories we have defined using the across domain classification there may be a stable risk attitude measurable from the PRA scale but not the GRA. Perhaps, the GRA with its focus on behavioural intentions (*what is the likelihood of engaging in this activity?*) does not provide a measure of the perceived risks involved and therefore cannot be used to indicate risk propensity in areas outside those measured in the DOSPERT. However, results of the PRA scale with its focus on risks (*how risky is this activity?*) across domains can be used as an indicator for a stable personality trait,

that is, assessors who can be categorized as belonging to the seeking-neutral group may be less conservative than those in the neutral-averse, averse and mixed groups and may view other life domains such as assessment of pharmaceutical drugs through this lens.

In the regression analysis the benefits and risk scores are explained by individual characteristics, namely personality traits and perceived risk attitude. We have shown in previous work that medical assessors' risk perception of the 3 medicinal drugs is specific to the situation under review: the type of product, the safety and ethical concerns, the number of patients potentially impacted by the adverse effects of the medicinal product along with individual characteristics such as years of experience as an assessor and gender (21). It now appears that personality traits also influence the perception of benefits and risks. It is surprising that Conscientiousness and Extraversion were the only personality traits from the BFI to be predictive of the benefit and the risk ratings respectively, as the other BFI personality traits (Openness, Neuroticism, and Agreeableness) have also been found to be predictive of increasing or depressing risk taking in other situations (10). Conscientiousness is described as the state of being thorough, careful, or vigilant; it implies a desire to do a task well and has been found to be influential of job performance(41, 42). Therefore, highly conscientious medical assessors may be sensitive to the promise of the benefits of medicinal products and may place great value on these aspects when reviewing a medical dossier. Gender was considered a potential confounder for the relationship between BFIC and the benefit ratings and the additive model constructed shows that indeed both variables contribute to explain the variance in the benefit ratings. The implication of these results, when the benefit risk assessment of medicinal drugs is carried out in teams as it is in Europe, is that careful thought should be given to the composition of personality traits and risk attitudes to minimize the negative effects on team processes of certain personality traits and

maximise the positive effects of others similar to the consideration given to the impact of cognitive styles on task execution (11, 43).

The authors believe that while assessors, by virtue of their training and experience in evaluating clinical data, are an important part of our regulatory system to protect the health of the public that there is also a human dimension that influences their views and this that is not negated simply by their expertise. Assessors are susceptible to the same failings as laypersons and this should be acknowledged within the regulatory process. The EMA within the BR Methodology project have taken steps in this direction and the Swine Flu case study provides one example of an 'ideal' decision making environment where 'hidden' or subconscious assumptions are made transparent. This does not mean the decision resulting from such a process will be considered 'right' but that every opportunity has been taken to increase the objectivity of the assessment and decrease the subjectivity inherent to any human decision making process.

This study, while providing important additional knowledge regarding benefit and risk perception of medicinal products and the interaction with individual and personality traits, has several limitations. The lack of predictive power of the GRA scale may be due to the specific risk taking activity questions found in the DOSPERT which may not fit the regulatory domain. In addition, the long duration of the study necessary for gathering data in this natural setting resulted in a 77% response rate by the final phase during which the BFI scale measurements were taken. The resulting sample of assessors within our study appears to be small however the authors hasten to point out that the seemingly small number of medical assessors is inherent in the design of the study as we wished to focus on assessors with expertise in specific disease areas. Nonetheless, future research could aim to enrol a larger sample of assessors to test the validity of the results and also to explore the impact of individual personality traits on group

decision making within the national agencies. Despite the above mentioned limitations our results remain useful for generating future hypotheses and are among the few available on expert medical assessors who are, understandably, not readily accessible for behavioural studies due to the confidential nature of their work and their heavy work commitments.

## **Conclusions**

There is a pervasive belief that decision making bodies, such as the European regulatory network by virtue of their organizational structure, allow for alternative perspectives to be rationally considered until the optimal decision is reached (44) i.e., relying on a hierarchical bottom-up flow of expert advice and consultation. There is, however, evidence to contradict this view, that is, real-life organizational decision making is prone to both cognitive and organizational limitations and that problems of ambiguity, uncertainty, conflict and individual risk attitudes and perceptions may negatively impact the elucidation and consideration of the alternatives(44). Our first contribution to the extensive body of work on risk perception is the observation that the perception of the benefits that accompany medicines is equally complex as that of the risks. As with laypersons, experts view benefits as negatively related to risks and there are reliable differences in how experts view benefits as well as risks. We encourage the investigation of benefit perception alongside that of risk perception. A second contribution is that experts perceive the risks of a hazard via a set of situational and individual characteristics and therefore the decision of what is risky is a complex interplay of the situation, their level of expertise, their perception of the risks involved and even their gender (6, 19, 45-47). The knowledge that individual characteristics such as personality traits may be influential in the way assessors perform their job is not surprising, like laypersons they are prone to biases and reliance on heuristics; however, it is important to provide empirical evidence of what maybe important

influences in the decision making process and to challenge those responsible to create diverse decision making teams where individual factors are appropriately balanced. The authors recommend that medical assessors within the national agencies participate in an evaluation that assesses their general risk attitudes and their personality traits. Workshops, similar to those conducted by the EMA Benefit –Risk Methodology Project to demonstrate the application of decision support tools, could be organized within the NCAs. The aim of the workshop should be to educate medical assessors on the evidence of risk perception, risk attitude and personality trait literature; to demonstrate the impact of their personality traits on decision making; to show how decision support tools can aid the transparency and minimize the impact of these traits.

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**Table 1. Demographic Characteristics**

<b>Variable</b>	<b>Characteristic</b>	<b>Frequency</b>	
<b>Gender</b>	Male	38	
	Female	37	
<b>Age</b>	Between 20 and 29	1	
	Between 30 and 39	22	
	Between 40 and 49	30	
	Between 50 and 59	18	
	Over 60	3	
<b>Professional Qualifications</b>	MD	27	
	MD/PhD	11	
	PhD	19	
	PhD/Pharm	3	
	Pharmacist	10	
	Other	5	
<b>Role in NCA</b>	CHMP member	6	
	Internal Assessor	57	
	External Assessor	9	
	Other	3	
<b>Years of Regulatory Experience by Country</b>	<b>Country</b>	<b>&lt;5 years</b>	<b>5+ years</b>
	France	2	8
	Spain	4	3
	The Netherlands	8	3
	United Kingdom	4	6
	Germany	3	7
	Austria	9	1
	Italy	10	0
	Ireland	0	3
	Portugal	1	3

**Table 2. Descriptive Statistics of DOSPERT Risk Taking by Domain**

	N	Mean	Std. Deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
Social Mean Score	75	5,3707	,78685	-,392	,277	-,251	,548
Financial Mean Score	75	2,3344	1,13292	1,119	,277	1,612	,548
Health Safety Mean Score	75	2,4200	,96771	1,010	,277	,866	,548
Recreational Mean Score	75	2,9542	1,16136	,423	,277	-,419	,548
Ethical Mean Score	75	1,8813	,76816	1,536	,277	3,594	,548
Valid N (listwise)	75						



**Table 3. DOSPERT Scale - Risk Taking and Risk Perception within the 5 Domains**

<b>Domain</b>	<b>Risk Seeking</b>		<b>Risk Neutral/Tolerant</b>		<b>Risk Averse</b>	
<b>Risk Taking</b>	<i>Row N=75</i>	<i>%</i>	<i>Row N=75</i>	<i>%</i>	<i>Row N=75</i>	<i>%</i>
Social	19	25.3	46	61.3	10	13.3
Financial	14	18.7	47	62.7	14	18.7
Health/Safety	9	12.0	57	71.0	9	12.0
Recreational	12	16.0	51	68.0	12	16.0
Ethical	14	18.7	53	70.7	8	10.7
<b>Risk Perception</b>						
	<i>Row N=75</i>	<i>%</i>	<i>Row N=75</i>	<i>%</i>	<i>Row N=75</i>	<i>%</i>
Social	9	12.0	53	70.7	13	17.3
Financial	13	17.3	48	64.0	14	18.7
Health/Safety	14	18.7	50	66.7	11	14.7
Recreational	13	17.3	46	61.3	16	21.3
Ethical	13	17.3	49	65.3	13	17.3

**Table 4. DOSPERT Scale - Risk Attitudes Across All Domains**

	General Risk Attitude (from the Risk Taking scale)		Perceived Risk Attitude (from the Risk Perception scale)	
	N=75	%	N=75	%
Seeking	2	2.5	2	2.5
Seeking Neutral	26	32.5	28	35.0
Neutral	12	15.0	14	17.5
Neutral Averse	24	30.0	25	31.2
Averse	0	0	2	2.5
Mixed	11	13.8	4	5.0

**Table 5. Correlation results between the DOSPERT Risk taking and Risk perception subscales**

Domain		
	<i>Spearman Rho</i>	<i>Significance (0.05)</i>
Social	-.149	.203
Financial	<b>-.343</b>	<b>.003</b>
Health/Safety	<b>-.357</b>	<b>.002</b>
Recreational	<b>-.470</b>	<b>.000</b>
Ethical	<b>-.350</b>	<b>.002</b>