ASIAN PACIFIC JOURNAL OF ALLERGY AND IMMUNOLOGY (2007) 25: 99-109

A Comparative Study of Patients' Preferences and Sensory Perceptions of Three Forms of Inhalers among Thai Asthma and COPD Patients

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SUMMARY In 9 study centers, 419 patients with asthma or COPD were randomized to receive two forms of salbutamol metered-dose-inhalers (MDIs), *i.e.* CFC-driven MDI, non-CFC (HFA) MDI and one salbutamol dry powder inhaler (DPI), in a multi-center, comparative, cross-over and randomized study, performed to facilitate the formulation of a strategic plan to phase out CFC MDIs. After having received all three forms of test products, the patients completed an evaluation questionnaire indicating their preferences, likelihood of treatment compliance on each product and the easiest one to use. Statistical analysis showed that the CFC MDI was significantly less irritating ($p < 0.014$) but lower in its overall appeal ($p < 0.0001$). The "most preferred form to be prescribed" was DPI at 47.5% followed by non-CFC at 32.5% and CFC MDI at 20.1%. Concerning the ease of use among the three forms of test products, 59.9% of the patients indicated "no difference". Adverse events were mild and occurred in only 8.2%. In conclusion, patients' preference and sensory perception among the three forms of inhalers were comparable except that the CFC MDI was significantly less irritating but lower in its overall appeal. DPI was the most preferred and easiest form to use but also the most expensive. Taking public health into consideration, a non-CFC MDI with a similar market price to the CFC MDI would be the obvious choice in a strategic plan to phase out CFC MDIs with the least difficulty to the consumers.

According to the Montreal Protocol, an international agreement, a total phase out of CFC production and use was set for the year 2000 for industrialized countries and for the year 2009 for most developing countries including Thailand.[1,2] Our Government through the Department of Industrial Works (DIW), the Allergy and Immunology Society of Thailand (AIST) with the cooperation of the Thai Food and Drug Administration (Thai FDA) has strategically planned to phase out CFC metered dose inhalers (CFC MDIs) with an adequate replacement by non-CFC MDIs commencing with the year 2006.

Currently, two types of MDIs, divided by the type of propellant into CFC and non-CFC MDIs, and one type of dry powdered inhalers (DPIs) without propellant, are available in Thailand. CFC was the first propellant used in MDIs for the treatment of asthma and chronic obstructive pulmonary diseases (COPD) in 1951.[3] It has been available in Thailand since 1984, followed by DPIs in 1990 and non-CFC, hydrofluoroalkane (HFA) MDIs in 1997. Hence, both physicians and patients are more familiar with

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CFC MDIs than the latter two forms because they have been in the market for a longer time.

HFAs, the non-chlorinated hydrofluoroalkanes, have been found and proven to be as safe for human use as CFC and were recommended as a suitable CFC substitute in MDIs for the last decade.[3,4] Efficacy, tolerability and safety of HFA propellant MDIs for both relieve and prevention in the treatment of asthma and COPD have been widely tested and proven by many studies to be similar to their CFC counterparts.[3,5-9] Initially, three forms of multidose DPIs were invented, i.e. turbuhaler, easyhaler and diskus, all of which delivered a comparable and consistent dose *in vitro*.[10] However, only two forms (turbuhaler and easyhaler) are still marketed. DPIs do not require a propellant but the user has to generate a sufficient inspiratory flow to actuate the device. DPIs are more expensive than CFC and HFA MDIs but they are regarded as an equivalent alternative.

In developed countries such as Australia, Canada, the European Union (EU) and Japan, where transition strategies have been completed, the CFC MDI phase-out was nevertheless complicated as it involved many factors *e.g.* medical, psychological, economical, availability and regulatory factors which were unique to each individual country.

The present status of availability and consumption of each form of MDI in Thailand as well as the future estimated consumption were investigated and reported earlier.[11] This report was used as background information to formulate the strategic National CFC phase out plan for MDIs in the country. Other points of concern, which may affect the consumer, were considered as well. These include 1) the preference for certain form of inhalers by both, patients and physicians, 2) the psychological effects such as adherence of patients and physicians to their most familiar form, i.e., CFC MDIs, and 3) the sensory perception of the patients when using different forms of inhalers such as the cooling effect, odor, taste, irritation etc.

In order to visualize these concerns, two studies were performed; the first study was a retrospective questionnaire survey to discover the problems encountered with MDIs, *i.e.* the practical, clinical and psychological aspects for both patients and physicians. This first study will be reported elsewhere.[12]

This article reports the second study, which aimed to compare the preferences and sensory perceptions of patients with asthma and COPD for the different forms of inhalers. The results of this study should facilitate the formulation of a strategic plan to phase out CFC MDIs with the least difficulty for all stakeholders.

MATERIALS AND METHODS

The study was conducted from June to September, 2004, at six teaching hospitals (five in the Bangkok Metropolitan Area, one in Chiang Mai); altogether nine sites participated (four pediatric clinics and five adult clinics).

Subjects

Asthma or COPD patients who met all inclusion criteria and did not exhibit any exclusion criteria were invited to participate in the study. The inclusion criteria comprised males and non-pregnant, non-lactating females, aged ≥ 9 years diagnosed with asthma or COPD who were able to participate in the study and who gave their informed consent. Parents or guardians gave informed consent for patients under 18 years old. The exclusion criteria were female patients with childbearing potential without using any birth control methods, those who had cardiovascular, hepatic, renal, neurological or other medical conditions that might significantly interfere with the study and those who regularly used medications for other conditions that might affect their ability to subjectively rate preferences and sensory perceptions of the drugs in the study. Patients who were having acute asthmatic attacks were also excluded.

Patients could be withdrawn from the study after enrollment for any of the following reasons: withdrawn consent, failure to follow specific protocol procedures and occurrence of an adverse event which affected the patient's participation in the study.

The clinical study was approved by the institutional ethical review boards of each study center.

Test products

Salbutamol inhalers were selected as study drug because of their popularity and availability in three forms: CFC-driven MDI (Buto Asma® 100 µg/puff), non-CFC (HFA) MDI (Ventolin evohaler® 100 µg/puff), and DPI (Buventol easyhaler® 100 µg/puff).

The Buto Asma® and Ventolin evohaler® were both aerosols, which contained a propellant and a drug; the actuator and mouthpiece were similar. The instructions how to deliver the medication and the directions for use were also the same. The Buventol easyhaler® was a dry powder inhaler; the appearance of the drug and its delivery technique are totally different from the aerosols. All of these drugs are available in the Thai market.

Study design and methods

The study was designed as a multicentered, comparative, cross-over, randomized and double-blinded study. The two MDIs were blinded to both the patient and the evaluator. Because of its obvious appearance, the DPI was blinded only to the evaluator.

Stage 1 Enrollment and informed consent. After the inclusion/exclusion criteria were reviewed, patients learned about the study by reading the information sheet and by discussing with the attending physician/research assistant, prior to completing the written informed consent. Demographic data and medical histories were recorded in the case record form (CRF) together with a physical examination, which included an assessment of the clinical status and vital signs.

Stage 2 Testing different forms of inhaler. This was done in a separate room for less interference. A randomized number was allocated to each test product. Each participant received one of the three products at a time for inhalation in a randomized fashion according to a balanced design. Each form was tested only once in random order.

Participants were given the evaluation questionnaire (Appendix 1) to read prior to the first test so that they knew what to evaluate. Then they were instructed by trained personnel to administer each type of test product correctly. Prior to inhaling each test product, the participants were asked to chew unsalted crackers then completely rinse out the cracker residues from their mouths with a cup of room-temperature water. Fifteen minutes after the administration of the test product, the patient's pulse was recorded and the evaluation questionnaire was filled in and checked for completeness by the research assistant. There were two 15-minute rest intervals (altogether 30 minutes) before the next test product was commenced. After the participants had completed inhaling the 3 forms of test products, the preference questionnaire (Appendix 2) was filled in. Any adverse events were also recorded.

The overall assessment of the test products was done using the Patient Evaluation Questionnaire. In this questionnaire, patients rated the test products on a 100-point visual analogue scale (VAS) for the following parameters: ease of use, amount of medicine reaching the bronchi, irritation, urge to cough, strength of odor, appeal of odor, strength of taste, appeal of taste, dry or moist sensation of the throat and overall appeal. In the Preference Questionnaire, participants were also asked about their preference and likelihood of treatment compliance for each product. Then, they were asked to compare the ease of use of each form of inhaler. Adverse events reported by the participants and changes in pulse rates which were recorded in the CRF 15 minutes after inhalation of each test product were considered safety parameters.

Data analysis

Differences in mean scores of each item (attribute rating) between the three test products were compared with repeated measures of analysis of variance (ANOVA) for total samples and for sample segments (*i.e.* different ages, genders and diagnoses). The chi-square (χ^2) test was used for the proportion data.

The above analysis plan was performed after the study data were completed and available for review, while the investigators and statistical team were still blinded to the test products. Statistical evaluation was done using the SPSS version 10.0.

RESULTS

A total of 420 patients participated in the study; 419 case record forms were completed for analysis. Among these participants, 105 (25.4%) were children (age ≥ 15 years), 188 (45.5%) adults (age 16-60 years) and 120 (29.1%) elders (age > 60 years). There were 212 (50.6%) female and 207 (49.4%) male patients with ages ranging from 9 to 94 years (mean ± SD = 43.5 ± 22.8 years).

Asthma was diagnosed in 360 patients, *i.e.* 136 (32.6%) asthma alone and 224 (53.7%) asthma with other diseases. Common associated diseases with asthma were allergic rhinitis (64.7%) and hypertension (17.9%). Only 57 (13.7%) were COPD patients, 2 patients had no diagnosis available. The duration of asthma ranged from 1 to 80 years, average of 12.5 ± 11.0 years. The severity of asthma (classified according to the GINA guideline)[13] was recorded in 234 patients. There were 100 (42.7%) mild intermittent, 111 (47.4%) mild persistent, 19 (8.1%) moderate and 4 (1.7%) severe persistent cases. The detailed demographic data are presented in Table 1.

Among the 419 participants, 410 (98.1%) had prior treatment with some form of MDIs. The numbers of patients who had ever used CFC, non-CFC MDIs or DPIs were 260 (63.4%), 212 (51.8%) and 219 (53.4%) respectively. Only 59 patients had ever used all three forms.

All patients had vital signs within normal range.[14,15] Changes in pulse rates before and after each test inhaler were observed as well as any events spontaneously reported by the patients. There was a significant difference in the pulse rate detected after non-CFC MDI use but the average value was still within normal limits, as shown in Table 2. Adverse events were reported by 8.2% of 1257 administrations of test drugs, 7.4% occurred after CFC, 10.7% after non-CFC and 6.4% after DPI use. These adverse events included dry throat, bitter taste, headache, throat irritation, nausea, numbness of lips or tongue and cough. Palpitation was also common but did not correlate with a change in pulse rates in most cases. Nevertheless, these symptoms were mild and easily tolerated; no patient had to withdraw because of these adverse events.

Table 1 Demographic data of participating patients (N = 419)

No.	Female	Male	Total
n	212	207	419
%	50.6	49.4	100.0
Mean age (years)	45.7 ± 18.8	41.2 ± 26.1	43.5 ± 22.8
Range (years)	9-78	9-94	9-94
Age groups (n = 413)			
Child (≤ 15 years)		105 (25.4%)	
Adult (16-60 years)		188 (45.5%)	
Old (> 60 years)		120 (29.1%)	
Diagnosis (n = 417)			
1. Asthma alone		136 (32.6%)	
2. Asthma and other diseases		224 (53.7%)	
Allergic rhinitis		145 (64.7%)	
Hypertension		40 (17.9%)	
Others*		39 (17.5%)	
3. COPD		57 (13.7%)	

**i.e.* diabetes mellitus 10 (4.5%), hypercholesterolemia 8 (3.6%), peptic ulcer 3 (1.3%), sinusitis 2 (0.9%), gout 2 (0.9%), hematologic disease 2 (0.9%), atopic dermatitis 2 (0.9%), bone disease 2 (0.9%), heart disease 2 (0.9%), and others such as coronary artery disease, Reiter's syndrome, pneumonitis, thyroiditis, hepatitis A infection , migraine, one each = 6 (2.7%).

Table 2 Pulse rates of patients before and after inhaling each test drug

	n	Mean ± SD	Range	*p*-value[a]
Before	418	80.0 ± 11.0	45-128	-
After CFC	417	79.5 ± 11.3	46-116	0.221
After Non CFC	417	79.2 ± 10.6	49-124	0.042
After DPI	417	79.5 ± 10.8	42-116	0.300

A, Paired T-test

Table 3 Perceptive experiences of participants after taking each form of inhaler

	N	CFC Mean ± SD	Non CFC Mean ± SD	DPI Mean ± SD	*p*- value[a]
Easy-to-use (VAS, 0 = easy, 100 = difficult)	**418**	23.8 ± 26.8	22.2 ± 25.6	21.2 ± 26.3	0.227
Medicine reaching the bronchi (VAS, 0 = none, 100 = extreme amount)	**418**	67.5 ± 25.2	70.1 ± 24.2	70.4 ± 26.7	0.087
Irritation (VAS, 0 = none, 100 = extreme irritation)	**418**	11.4 ± 19.6	12.8 ± 21.0	14.8 ± 23.1	**0.014**
Urge to cough (VAS, 0 = none, 100 = strong urge)	**418**	9.0 ± 17.4	9.8 ± 19.8	9.0 ± 17.6	0.695
Able to detect an odor	**417**	158 (37.9%) yes*****	161 (38.6%) yes******	119 (28.5%) yes	**< 0.0001**[b]
Strength of odor (VAS, 0 = none, 100 = strong odor)	**37**	36.4 ± 23.1	41.5 ± 29.9	36.8 ± 27.6	0.674
Like the odor (VAS, 0=dislike, 100=like)	**38**	48.7 ± 25.3	53.9 ± 27.5	55.6 ± 25.7	0.365
Able to detect a taste, (yes)	**417**	231 (55.4%)	206 (49.4%)	258 (61.7%)	**< 0.0001**[b]
Strength of taste (VAS, 0 = none, 100 = strong taste)	**127**	39.4 ± 27.7	40.1 ± 27.6	38.0 ± 27.9	0.751
Like the taste (VAS, 0 = dislike, 100 = like)	**127**	51.4 ± 28.4	55.0 ± 57.1	53.8 ± 31.4	0.692
Dry or moist (VAS, 0 = dry, 100 = moist)	**414**	16.9 ± 24.1	16.1 ± 24.8	17.8 ± 25.8	0.478
Overall liking (VAS, 0 = dislike, 100 = like most)	**416**	57.1 ± 27.3	62.7 ± 25.7	62.7 ± 27.4	**< 0.0001**

A, Repeated measures ANOVA; VAS, Visual analog scale; b, χ^2 test; ***,**** $p = 0.001$ *vs*. DPI

The mean attribute ratings for each item in the evaluation questionnaires for each form of inhaler are presented in Table 3 (questions 1 to 11 in Appendix 1). Statistical analysis of the mean attribute ratings by repeated measurement ANOVA showed that CFC MDIs were significantly less irritating ($p < 0.014$) but lower in overall appeal ($p < 0.0001$). The "most preferred form to be prescribed" was DPI at 47.5% followed by non-CFC at 32.5%, and CFC MDIs at 20.1% (questions 1 and 2 in Appendix 2) (Table 4).

Table 4 Overall preference and compliance of the participants evaluated from responses to the preference questionnaire (Appendix 2, Nos. 1 and 2)

Inhaler evaluation	Number of responses n (%)		
	CFC	Non-CFC	DPI
Ranking the form of inhalers patients preferred to be prescribed			
▪ The highest preference (n = 418)	84 (20.1)	136 (32.5)	**198 (47.5)**
▪ The second preference (n = 418)	170 (40.7)	165 (39.5)	83 (19.9)
▪ The least preference (n = 417)	162 (38.8)	117 (28.1)	138 (33.1)

Compliance to the prescription	The most preferred form	The second preferred	The least preferred
▪ Definitely comply	**375 (89.5)**	280 (66.8)	222 (53.0)
▪ Probably comply	34 (8.1)	113 (27.0)	102 (24.3)
▪ Probably not comply	8 (1.9)	18 (4.3)	63 (15.0)
▪ Definitely not comply	2 (0.5)	8 (1.9)	32 (7.6)
p-value[a]	< 0.0001	< 0.0001	< 0.0001

A, χ^2 test

Table 5 Some differences of CFC, non-CFC (HFA) metered dose inhalers and dry powder inhalers

	CFC MDIs	Non-CFC MDIs	DPIs
Ease of use	More difficult, need hand-mouth co-ordination	Same as CFC MDIs	Easier, breath-actuated
Aftertaste feeling	Cool	Less cool, finer and slower and feel softer	Little irritation
Propellant	CFCs	HFAs	No propellant
	Ozone depleting potential	No damage to ozone layer	Need sufficient inspiratory flow to actuate DPIs
	Global warming potential = 1	Global warming potential = 0.26	
	Atmospheric life CFC_{11} = 60 years	Atmospheric life HFA134a = 16 years	
Presentation	Suspension	Solution	Powder
Surfactant	+	±	
Cost	Comparable to non-CFC MDIs	Comparable to CFC MDIs	More expensive

CFC, chlorofluorocarbon; MDIs, metered dose inhalers; HFA, hydrofluoroalkane; DPIs, dry powder inhalers.

When the "most preferred form" was prescribed, 89.5% of the patients stated that they would definitely comply with the prescription, whereas only 66.8% and 53.0% of the patients said they would comply when the second and the third preferred drugs were prescribed; these data clearly showed a significant difference in patients' compliance ($p < 0.0001$) (Table 4).

The results imply that if inhaled drugs are needed, patients should take part in the selection; otherwise compliance to the prescription may be poor. There was no significant difference in patients' preference and compliance with regards to the sequence of administration of the three forms of inhalers.

Concerning the ease of use (question 3 in Appendix 2), 59.9% of the patients found "no difference" between the test products indicating that they were equally easy (74.0%), equally moderately easy (25.2%) and equally difficult to use (0.8%).

Among the 40.1% of patients, who stated that the ease of use was different for each inhaler device, DPI was the easiest (58.2%), followed by non-CFC (27.7%) and CFC MDIs (14.1%).

DISCUSSION

A comparison of the clinical efficacy of different inhaler devices for the delivery of short-acting β_2-bronchodilators and of corticosteroids (ICS) either with or without a spacer, by means of a meta analysis of 81 randomized controlled trials by Brockelbank, *et al.*[16] in 2001 revealed no significant difference. However, there are some differences between CFC, non-CFC MDIs and DPIs as shown in Table 5. CFC-free inhalers may taste slightly different and feel less cold than those containing CFCs, moreover the spray is finer and slower and gives a softer feeling on the back of the throat. Usually the dose of active ingredients in each "puff" is the same except for Qvar® (Beclomethasone dipropionate) which contains half the dose of other equivalent MDIs. The aerosol droplets of Qvar® are smaller than those of other aerosols, enhancing the deposition of medication in the lungs.[17-20]

This study demonstrated that patients evaluated various sensory factors as non significant when comparing the three forms of inhalers except for "irritation" which was significantly less for CFC MDIs. But the overall appeal of DPIs and non-CFC MDIs were preferred to that of CFCs, which may be due to other favourable sensory perceptions of these two forms. It must also be taken into consideration that the results of this clinical study were observations after only one-time administration of the inhalers, and that there was no follow-up assessment of either symptom relief or any changes in the sensory perception after long-term use. However, patients, who have ever used the three forms of inhaler in their daily life also gave similar responses.[12]

DPI seems to be the most preferred formulation and achieved the best compliance. Good compliance is very important when selecting inhalers for long-term treatment, especially in chronic diseases such as asthma and COPD. Moreover, this study revealed that the majority of the participating patients did not know that CFC was either harmful to the environment or that CFC was one of the components in their inhalers. In addition, they had little concern about the "harmful effect to the environment" when choosing their inhalers. This information confirms the need for educating patients and the general public as a whole.

Statistical analysis for each sample segment was performed for 3 subgroups of participants. The first subgroup was divided according to age into those 15 years or under, 16-60 years and over 60 years old. The second subgroup compared females *vs.* males and the third subgroup contained asthma *vs.* COPD patients. The detailed data will be reported separately. In summary, the three subgroups revealed similar results to the total subjects. However, the overall trend showed a higher preference for non-CFC MDIs in children and for DPI in the old age group.

The results obtained from our previous two studies[11,12] served as basic information for the development of a strategic plan on harmonization for phasing out CFC MDIs. It is also noted in Losey's recommendation about National CFC MDI Transition Strategy Options in 2002 that developing and implementing an effective transition strategy takes time and effort. The first step which the US FDA took in the planning and regulatory process for the eventual transition from CFC MDIs to non-CFC alternatives started by publishing an Advance Notice of Proposed Rulemaking (ANPR) in various media in March, 1997. With this ANPR, the US FDA proposed a process for the transition in order to obtain public input and then setting criteria and procedures in the USA Transition Strategy. After 5 years, the phase-out decisions were finally issued in July 2002, and came into effect in January 2003.[21-23]

So in general, the phase out process of CFC MDIs should comprise 2 parts: an educational program and a phase out decision with regulatory enforcement. Thailand has successfully completed these processes at the end of 2005.

In conclusion, a comparison of patients' preferences and sensory perceptions among the three forms of inhalers revealed that irritation was the only significant difference in the patients' perception. DPIs appeared to be the most preferred and easiest form to use. If the most preferred form of inhaler was prescribed, 89.5% of the patients would definitely comply with prescriptions. These findings suggest that DPI may be the best choice of the three forms when long-term compliance is considered. However, the price of DPI in the market is still three to four times higher than of the other two inhaler forms. Taking into consideration the market price and the national public health administration, the HFA-MDI is obviously a preferable alternative to the CFC-MDI.

ACKNOWLEDGEMENTS

This study was part of consultant services conducted by the Allergy and Immunology Society of Thailand for Harmonization Phase-out of MDIs using CFC as Propellant in Thailand. The project was supported by the Thailand National CFC Phase-out Plan and coordinated by the Project Management Unit, Department of Industrial Works.

The authors thank the following colleagues who contributed to the study as co-investigators at each study site : Ngamphaiboon J, Ruxrungtham K, Chantaphakul H, from Chulalongkorn Hospital; Fuangtong R, Suttithawil W, Sangasapaviliyah A, from Pramongkutklao Hospital; Janwityanujit S, Kiatboonsri S, Pornsuriyasak P, Direkwattanachai C, Benjaponpitak S, from Ramathibodi Hospital; Vichyanond P, Piboonpocanun O, Dejsomritrutai W, Thongngarm T, Luangwedchakarn V, from Siriraj Hospital; Vangveeravong M, from the Queen Sirikit National Institute of Child Health; Phothirat C, Deesomchok A, from the Faculty of Medicine, Chiang Mai University.

The authors would also like to thank Professor Visanu Thamlikitkul and Mr. Suthipol Udompanthurak for their statistical advice and our research assistants: Ms. Bangorn Pinkaew and Ms. Siriporn Phoemsa.

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Appendix 1

Name..... HN..... Patient Number..... Date.....

Patient Evaluation Questionnaire: After first test product **(A)**

How **easy** is it to use this inhaler?

Very easy 0 — Very difficult 100

Upon inhalation

1. How much medicine reaches your bronchi?

None at all 0 — An extreme amount 100

2. How much **IRRITATION** do you feel?

None at all 0 — An extreme irritation 100

3. How **STRONG** is the **URGE to COUGH**

No urge at all 0 — Extremely strong urge 100

4. Do you detect an **ODOUR**?

❑ Yes ❑ No

If you check **Yes**, continue with questions 5 and 6
If you check **No**, skip to question 7

5. How **STRONG** is the **ODOUR** of the product?

No odour at all 0 — Extremely strong odour 100

6. How much do you **LIKE** the **ODOUR** of the product?

Dislike it extremely 0 — Like it extremely 100

7. Do you detect a **TASTE**?

❑ Yes ❑ No

If you check **Yes**, continue with questions 8 and 9
If you check **No**, skip to question 10

8. How **STRONG** is the **TASTE** of the product?

No taste at all 0 — Extremely strong taste 100

9. How much do you **LIKE** the **TASTE** of the product?

Dislike it extremely 0 — Like it extremely 100

10. After inhalation, describe how **DRY** or **MOIST** your throat feel?

Extremely dry 0 — Extremely moist 100

11. OVERALL, how much do you **LIKE** this product?

Dislike it extremely 0 — Like it extremely 100

After inhalation

Do you have any adverse symptoms?

❑ No ❑ Yes, please describe .....

Appendix 2

Patient Number_____

Patient Preference Questionnaire
(Overall Evaluation)

(Please mark ✓ in front of the statement which you think is appropriate.)

1. From the 3 forms of inhaled drugs which you have tried today, rank the test products according to which you would prefer your doctor prescribe.

   - Prefer **MOST** to be prescribed
     - ❑ 1st test product
     - ❑ 2nd test product
     - ❑ 3rd test proudct
   - Prefer **SECOND** to be prescribed
     - ❑ 1st test product
     - ❑ 2nd test product
     - ❑ 3rd test proudct
   - Prefer **LEAST** to be prescribed
     - ❑ 1st test product
     - ❑ 2nd test product
     - ❑ 3rd test proudct

2. Your doctor has told you that you must use inhaled drugs every day. For each of the test product you have tried today, how likely are you to comply with the doctor's prescription?

   - For the inhaler you prefer **MOST to be prescribed**, would you
     - ❑ Definitely comply with the prescription
     - ❑ Probably comply with the prescription
     - ❑ Probably not comply with the prescription
     - ❑ Definitely not comply with the prescription
   - For the inhaler you prefer **SECOND to be prescribed**, would you
     - ❑ Definitely comply with the prescription
     - ❑ Probably comply with the prescription
     - ❑ Probably not comply with the prescription
     - ❑ Definitely not comply with the prescription
   - For the inhaler you prefer **LEAST to be prescribed**, would you
     - ❑ Definitely comply with the prescription
     - ❑ Probably comply with the prescription
     - ❑ Probably not comply with the prescription
     - ❑ Definitely not comply with the prescription

3. Please compare the **ease of use** between each form of test products you have tried today?

   - ❑ Not different
     - ❑ equally easy
     - ❑ equally moderately easy
     - ❑ equally difficult
   - ❑ Different

   Please indicate the number which you think appropriate in front of each test product. (1 = easiest to use, 2 = moderately, 3 = the most difficult)

   - ❑ 1st test product
   - ❑ 2nd test product
   - ❑ 3rd test product