

#### **Clinical trial results:**

A Randomized, Evaluator-Blind, Crossover, Single Dose Study of the Bronchodilator Effect of Formoterol Fumarate in Combination With Mometasone Furoate Metered Dose Inhaler Delivered With and Without a Spacer Versus Placebo and Foradil® Aerolizer® in Children With Persistent Asthma (Protocol No. P06476)

Summary	y
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EudraCT number	2014-004582-24
Trial protocol	Outside EU/EEA
Global end of trial date	15 October 2011
Results information	
Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	30 July 2015

#### **Trial information**

Trial identification	
Sponsor protocol code	P06476
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01258803
WHO universal trial number (UTN)	-
Other trial identifiers	Merck protocol number: MK-0887A-178

Notes:

Sponsors	
Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage	
Analysis stage	Final
Date of interim/final analysis	15 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 October 2011
Global end of trial reached?	Yes
Global end of trial date	15 October 2011
Was the trial ended prematurely?	No

Notes:

#### General information about the trial

Main objective of the trial:

A study to compare the bronchodilatory effect of a single dose of Mometasone Furoate/Formoterol Fumarate (MF/F) pressurized metered dose inhaler (MDI) delivered with and without an AeroChamber Plus® with Flow-Vu® Anti-Static Valved Holding Chamber (spacer) versus Placebo MDI (combined with and without spacer) and formoterol fumarate (F) dry powder inhaler (DPI). Participants were randomly assigned to 1 of 6 treatment sequences and each participant was to receive a single dose of each of 4 treatments in each period. Each treatment period was separated by a 5 to 7 day washout period. It assumed that a single dose MF/F MDI 100/10 mcg delivered with a spacer would produce bronchodilation, defined as a significant increase in forced expiratory volume in one second (FEV1) area under the curve from 0 to 12 hours (AUC[0-12 hr]) when compared to placebo.

#### Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -	
Actual start date of recruitment	08 December 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

# Population of trial subjects Subjects enrolled per country Country: Number of subjects enrolled United States: 92 Worldwide total number of subjects 92

0

Notes:

EEA total number of subjects

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	92

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

### **Subject disposition**

#### Recruitment

Recruitment details:

Participants were recruited from 28 study sites in the United States. Primary Therapy Period: December 2010 to October 2011.

#### **Pre-assignment**

Screening details:

The study included a 4-week Run-In Period during which participants were treated with Mometasone

Period 1	
	Treatment Period 1 (1 dose)
	Yes
·	Randomised - controlled
	Single blind
_	Investigator <sup>[1]</sup>
Arms	
Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1
Arm description:	
	se Inhaler (MDI) with spacer, Treatment Period 2: Mometasone I without spacer, Treatment Period 3: MF/F MDI with spacer, r (DPI)
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate [	DPI 10 mcg administered as a single dose
	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Dosage and administration details: Two inhalations of Mometasone Furoate/R	Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)
Dosage and administration details: Two inhalations of Mometasone Furoate/Fidose without an AeroChamber Plus® Flow Investigational medicinal product name	
Dosage and administration details: Two inhalations of Mometasone Furoate/Fidose without an AeroChamber Plus® Flow Investigational medicinal product name	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Dosage and administration details: Two inhalations of Mometasone Furoate/Fidose without an AeroChamber Plus® Flow Investigational medicinal product name Investigational medicinal product code	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Dosage and administration details: Two inhalations of Mometasone Furoate/Fdose without an AeroChamber Plus® Flow Investigational medicinal product name Investigational medicinal product code Other name	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

	T
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spa	rered as a single dose with an AeroChamber Plus® Flow-Vu® acer)
Arm title	Treatment Sequence 2
Arm description:	
Treatment Period 1: F DPI, Treatment Period 4: Pl	eriod 2: MF/F MDI without spacer, Treatment Period 3: MF/F acebo MDI with spacer
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	·
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Mometasone Furoate	/Formoterol Fumarate MDI 50/5 mcg administered as a single
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo	/Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo Investigational medicinal product name	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name	w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A
Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	ww-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution
Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate,	ww-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  (Formoterol Fumarate MDI 50/5 mcg administered as a single
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-\ Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer
Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate, dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer  Inhalation solution
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration Dosage and administration details: Two inhalations of placebo MDI administ	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer  Inhalation use  Inhalation solution  Inhalation solution  Inhalation use
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details:	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer  Inhalation use  Inhalation solution  Inhalation solution  Inhalation use
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-\ Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spa	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer  Inhalation solution Inhalation solution Inhalation solution Inhalation solution Inhalation use
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration Dosage and administration Arm title Arm description: Treatment Period 1: MF/F MDI without s	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer  Inhalation use  Inhalation solution  Inhalation solution  Inhalation solution  Inhalation solution  Inhalation use  Pered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 3
Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration Dosage and administration details: Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spatartitle) Arm description:	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer  Inhalation use  Inhalation solution  Inhalation solution  Inhalation solution  Inhalation solution  Inhalation use  Pered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 3

Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	/Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (sp	tered as a single dose with an AeroChamber Plus® Flow-Vu® acer)
Anti-Static Valved Holding Chamber (sp. Arm title  Arm description:	Treatment Sequence 4
Anti-Static Valved Holding Chamber (sp. Arm title  Arm description:	Treatment Sequence 4  ut spacer, Treatment Period 2: MF/F MDI with spacer, Treatmen
Arm title  Arm description: Treatment Period 1: Placebo MDI without	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental
Anti-Static Valved Holding Chamber (sp. Arm title  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF	Treatment Sequence 4  ut spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer
Anti-Static Valved Holding Chamber (sp.  Arm title  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental
Anti-Static Valved Holding Chamber (sp.  Arm title  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental  Formoterol Fumarate DPI
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms  Routes of administration  Dosage and administration details:	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms  Routes of administration  Dosage and administration details:	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product name Investigational medicinal product code Other name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Arm title	Treatment Sequence 6		
Arm description:			
Treatment Period 1: MF/F MDI with spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 4: F DPI			
Arm type	Experimental		
Investigational medicinal product name	Formoterol Fumarate DPI		
Investigational medicinal product code			
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®		
Pharmaceutical forms	Inhalation powder		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose		
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer		
Investigational medicinal product code			
Other name	SCH 418131, MK-0877A		
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)			
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer		
Investigational medicinal product code			
Other name	SCH 418131, MK-0877A		
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)			
Investigational medicinal product name	Placebo MDI without spacer		
Investigational medicinal product code			
Other name			
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew the treatment assignment of each subject.

Number of subjects in period 1	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	15	16	15
Completed	15	16	15

Number of subjects in period 1	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	16
Completed	15	15	16

Period 2	_	
Period 2 title	Treatment Period 2 (1 dose)	
Is this the baseline period?	No	
Allocation method	Randomised - controlled	
Blinding used	Single blind	
Roles blinded	Investigator <sup>[2]</sup>	
Arms		
Are arms mutually exclusive?	Yes	
Arm title	Treatment Sequence 1	
Arm description:		
Treatment Period 1: Placebo MDI with sp Period 3: MF/F MDI with spacer, Treatme	pacer, Treatment Period 2: MF/F MDI without spacer, Treatment ent Period 4: F DPI	
Arm type	Experimental	
Investigational medicinal product name	Formoterol Fumarate DPI	
Investigational medicinal product code		
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®	
Pharmaceutical forms	Inhalation powder	
Routes of administration	Inhalation use	
Dosage and administration details:		
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Investigational medicinal product code		
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
	/Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer	
Investigational medicinal product code		
0.1	SCH 418131, MK-0877A	
Other name	·	
Pharmaceutical forms	Inhalation solution	

Dosage and administration details:		
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)		
Investigational medicinal product name		
Investigational medicinal product code	·	
Other name		
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)		
Arm title	Treatment Sequence 2	
Arm description:		
-	eriod 2: MF/F MDI without spacer, Treatment Period 3: MF/F acebo MDI with spacer	
Arm type	Experimental	
Investigational medicinal product name	Formoterol Fumarate DPI	
Investigational medicinal product code		
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®	
Pharmaceutical forms	Inhalation powder	
Routes of administration	Inhalation use	
Dosage and administration details:		
	DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Investigational medicinal product code	·	
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
	Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer	
Investigational medicinal product code		
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)		
Investigational medicinal product name	Placebo MDI with spacer	
Investigational medicinal product code		
Other name		
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)		
Arm title	Treatment Sequence 3	
Arm description:		
Treatment Period 1: MF/F MDI without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo MDI with spacer, Treatment Period 4: MF/F MDI with spacer		
Arm type	Treatment Sequence	

Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	/Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (sp	tered as a single dose with an AeroChamber Plus® Flow-Vu® acer)
Anti-Static Valved Holding Chamber (sp. Arm title  Arm description:	Treatment Sequence 4
Anti-Static Valved Holding Chamber (sp. Arm title  Arm description:	Treatment Sequence 4  ut spacer, Treatment Period 2: MF/F MDI with spacer, Treatmen
Arm title  Arm description: Treatment Period 1: Placebo MDI without	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental
Anti-Static Valved Holding Chamber (sp. Arm title  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF	Treatment Sequence 4  ut spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer
Anti-Static Valved Holding Chamber (sp.  Arm title  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental
Anti-Static Valved Holding Chamber (sp.  Arm title  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental  Formoterol Fumarate DPI
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms  Routes of administration  Dosage and administration details:	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type  Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms  Routes of administration  Dosage and administration details:	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment F/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Arm title  Arm description: Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product name Investigational medicinal product code Other name	Treatment Sequence 4  It spacer, Treatment Period 2: MF/F MDI with spacer, Treatment/F MDI without spacer  Experimental  Formoterol Fumarate DPI  SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder  Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
·	with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	•
Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spa	tered as a single dose without an AeroChamber Plus® Flow-Vu(acer)
Arm title	Treatment Sequence 5
Arm description:	•
Treatment Period 1: MF/F MDI without s MDI with spacer, Treatment Period 4: Pl	spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F acebo MDI without spacer
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	1 111111111111
Two inhalations of Mometasone Furoate,	/Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	•
	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	1 22 22
-	tared as a single dose without an AeroChamber Plus® Flow Vu

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu®

Arm title	Treatment Sequence 6
Arm description:	
Treatment Period 1: MF/F MDI with space Period 3: MF/F MDI without spacer, Treatment Period 3: MF/F MDI without spacer, Treatment Period 1: MF/F MDI without spacer, Treatment Period 1: MF/F MDI with spacer Period 3: MF/F MDI without spacer Per	er, Treatment Period 2: Placebo MDI without spacer, Treatment atment Period 4: F DPI
Arm type	Treatment Sequence
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	

Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew the treatment assignment of each subject.

Number of subjects in period 2	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	15	16	15
Completed	14	14	15
Not completed	1	2	0
Consent withdrawn by subject	-	1	-
Protocol deviation	1	1	-

Number of subjects in period 2	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	16
Completed	15	15	15
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Protocol deviation	-	-	1

Period 3		
Period 3 title	Treatment Period 3 (1 dose)	
Is this the baseline period?	No	
Allocation method	Randomised - controlled	
Blinding used	Single blind	
Roles blinded	Investigator <sup>[3]</sup>	
Arms		
Are arms mutually exclusive?	Yes	
Arm title	Treatment Sequence 1	
A describetions	<u> </u>	

#### Arm description:

Treatment Period 1: Placebo Metered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometasone Furoate/Formoterol Fumarate (MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer, Treatment Period 4: F Dry Powder Inhaler (DPI)

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

#### Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
dose with an AeroChamber Plus® Flow-	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spa	ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)
Arm title	Treatment Sequence 2
Arm description:	
Treatment Period 1: F DPI, Treatment Pe MDI with spacer, Treatment Period 4: Pl	eriod 2: MF/F MDI without spacer, Treatment Period 3: MF/F acebo MDI with spacer
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
	SCH 418131, MK-0877A Inhalation solution
Pharmaceutical forms	
Routes of administration	Inhalation solution
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/ dose without an AeroChamber Plus® Flo	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo  Investigational medicinal product name  Investigational medicinal product code	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/	Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-N	Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-V Investigational medicinal product name	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-\ Investigational medicinal product name Investigational medicinal product code	Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-Investigational medicinal product name Investigational medicinal product code Other name	Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)  Placebo MDI with spacer
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate/dose with an AeroChamber Plus® Flow-\ Investigational medicinal product name Investigational medicinal product code	Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)

Two inhalations of placebo MDI administered as a single dose with an AeroChamber Plus® Flow-Vu®

Arm title	Treatment Sequence 3
Arm description:	
Treatment Period 1: MF/F MDI without s MDI with spacer, Treatment Period 4: MI	pacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo F/F MDI with spacer
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Other name Pharmaceutical forms	Inhalation solution
	Inhalation solution Inhalation use
Pharmaceutical forms	
Pharmaceutical forms Routes of administration Dosage and administration details:	Inhalation use ered as a single dose with an AeroChamber Plus® Flow-Vu®
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of placebo MDI administ	Inhalation use ered as a single dose with an AeroChamber Plus® Flow-Vu®
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administration Chamber (spa	Inhalation use ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (space of the control of th	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (space Arm title)  Arm description:  Treatment Period 1: Placebo MDI without	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administration Anti-Static Valved Holding Chamber (spanned Arm title)  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spanned at the second at	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer  Experimental
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spate Arm title)  Arm title  Arm description:  Treatment Period 1: Placebo MDI withou Period 3: F DPI, Treatment Period 4: MF, Arm type  Investigational medicinal product name	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer  Experimental
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spanned and the second and	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer  Experimental  Formoterol Fumarate DPI

Dosage and administration details:		
	DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Investigational medicinal product code		
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
	/Formoterol Fumarate MDI 50/5 mcg administered as a single pw-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer	
Investigational medicinal product code		
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI without spacer	
Investigational medicinal product code		
Other name		
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:	•	
Two inhalations of placebo MDI administratic Valved Holding Chamber (spa	ered as a single dose without an AeroChamber Plus® Flow-Vu®acer)	
Arm title	Treatment Sequence 5	
Arm description:		
Treatment Period 1: MF/F MDI without s MDI with spacer, Treatment Period 4: Pl	spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F acebo MDI without spacer	
Arm type	Experimental	
Investigational medicinal product name	Formoterol Fumarate DPI	
Investigational medicinal product code		
Other name		
	SCH 045571, MK-5571, Foradil® Aerolizer®	
Pharmaceutical forms	SCH 045571, MK-5571, Foradil® Aerolizer®  Inhalation powder	
Pharmaceutical forms  Routes of administration	Inhalation powder	
Routes of administration		
Routes of administration  Dosage and administration details:	Inhalation powder Inhalation use	
Routes of administration  Dosage and administration details:	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product code	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name  Investigational medicinal product code Other name	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A Inhalation solution	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate,	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A Inhalation solution Inhalation use	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate,	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer	
Routes of administration  Dosage and administration details: Two inhalations of Formoterol Fumarate Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate, dose without an AeroChamber Plus® Flo	Inhalation powder Inhalation use  DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)	

Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose with an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)			
Investigational medicinal product name	Placebo MDI without spacer		
Investigational medicinal product code			
Other name			
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)			
Arm title	Treatment Sequence 6		
Arm description:			
Treatment Period 1: MF/F MDI with space Period 3: MF/F MDI without spacer, Treatment	er, Treatment Period 2: Placebo MDI without spacer, Treatment tment Period 4: F DPI		
Arm type	Experimental		
Investigational medicinal product name	Formoterol Fumarate DPI		
Investigational medicinal product code			
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®		
Pharmaceutical forms	Inhalation powder		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose		
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer		
Investigational medicinal product code			
Other name	SCH 418131, MK-0877A		
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)			
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer		
Investigational medicinal product code			
Other name	SCH 418131, MK-0877A		
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			
	Formoterol Fumarate MDI 50/5 mcg administered as a single (u® Anti-Static Valved Holding Chamber (spacer)		
Investigational medicinal product name	Placebo MDI without spacer		
Investigational medicinal product code			
Other name			
Pharmaceutical forms	Inhalation solution		
Routes of administration	Inhalation use		
Dosage and administration details:			
Two inhalations of placebo MDI administered as a single dose without an AeroChamber Plus® Flow-Vu®			

Anti-Static Valved Holding Chamber (spacer)

[3] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew

Number of subjects in period 3	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	14	14	15
Completed	14	14	14
Not completed	0	0	1
Protocol deviation	-	-	1

Number of subjects in period 3	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	15
Completed	15	15	15
Not completed	0	0	0
Protocol deviation	-	-	-

Period 4	
Period 4 title	Treatment Period 4 (1 dose)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator <sup>[4]</sup>
Arms	
Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1
Arm description:	
Treatment Period 1: Placebo MDI w	with spacer, Treatment Period 2: MF/F MDI without spacer, Treatment

Treatment Period 1: Placebo MDI with spacer, Treatment Period 2: MF/F MDI without spacer, Treat	ment
Period 3: MF/F MDI with spacer, Treatment Period 4: F DPI	

Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

#### Dosage and administration details:

Two inhalations of Formoterol Fumarate DPI 10 mcg administered as a single dose

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

#### Dosage and administration details:

Two inhalations of Mometasone Furoate/Formoterol Fumarate MDI 50/5 mcg administered as a single dose without an AeroChamber Plus® Flow-Vu® Anti-Static Valved Holding Chamber (spacer)

Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spa	ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)
Arm title	Treatment Sequence 2
	eriod 2: MF/F MDI without spacer, Treatment Period 3: MF/F
MDI with spacer, Treatment Period 4: Pl	Treatment Sequence
Arm type	
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	COLLOAFEZI MICEFZI Farradile Apraliane
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	

Other name

Arm title	Treatment Sequence 3
Arm description:	
Treatment Period 1: MF/F MDI without s MDI with spacer, Treatment Period 4: MI	pacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo F/F MDI with spacer
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI with spacer
Investigational medicinal product code	
Othername	
Other name	
Pharmaceutical forms	Inhalation solution
	Inhalation solution Inhalation use
Pharmaceutical forms	
Pharmaceutical forms Routes of administration Dosage and administration details:	Inhalation use ered as a single dose with an AeroChamber Plus® Flow-Vu®
Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of placebo MDI administ	Inhalation use ered as a single dose with an AeroChamber Plus® Flow-Vu®
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administration Chamber (spa	Inhalation use ered as a single dose with an AeroChamber Plus® Flow-Vu®
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (space of the control of th	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (space Arm title)  Arm description:  Treatment Period 1: Placebo MDI without	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administration Anti-Static Valved Holding Chamber (spanned Arm title)  Arm description:  Treatment Period 1: Placebo MDI without Period 3: F DPI, Treatment Period 4: MF	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spanned at the second at	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer  Treatment Sequence
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spate Arm title)  Arm title  Arm description:  Treatment Period 1: Placebo MDI withou Period 3: F DPI, Treatment Period 4: MF, Arm type  Investigational medicinal product name	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer  Treatment Sequence
Pharmaceutical forms  Routes of administration  Dosage and administration details:  Two inhalations of placebo MDI administ Anti-Static Valved Holding Chamber (spanned and the second and	Inhalation use  ered as a single dose with an AeroChamber Plus® Flow-Vu® acer)  Treatment Sequence 4  t spacer, Treatment Period 2: MF/F MDI with spacer, Treatment /F MDI without spacer  Treatment Sequence  Formoterol Fumarate DPI

Dosage and administration details:		
	DPI 10 mcg administered as a single dose	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Investigational medicinal product code		
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
	/Formoterol Fumarate MDI 50/5 mcg administered as a single pw-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer	
Investigational medicinal product code		
Other name	SCH 418131, MK-0877A	
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:		
	/Formoterol Fumarate MDI 50/5 mcg administered as a single Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name	Placebo MDI without spacer	
Investigational medicinal product code		
Other name		
Pharmaceutical forms	Inhalation solution	
Routes of administration	Inhalation use	
Dosage and administration details:	•	
Two inhalations of placebo MDI administratic Valved Holding Chamber (sp.	tered as a single dose without an AeroChamber Plus® Flow-Vu® acer)	
Arm title	Treatment Sequence 5	
Arm description:		
Treatment Period 1: MF/F MDI without s MDI with spacer, Treatment Period 4: Pl	spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F lacebo MDI without spacer	
Arm type	Treatment Sequence	
Investigational medicinal product name	Formoterol Fumarate DPI	
Investigational medicinal product code		
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®	
Pharmaceutical forms	Inhalation powder	
Routes of administration	Inhalation use	
Dosage and administration details:		
<u> </u>		
I WO INITIALIZATIONS OF FORMOTEROL FUMARATE	DPI 10 mcg administered as a single dose	
Investigational medicinal product name	DPI 10 mcg administered as a single dose  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Investigational medicinal product name		
Investigational medicinal product name Investigational medicinal product code	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer	
Investigational medicinal product name Investigational medicinal product code Other name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A	
Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A  Inhalation solution	
Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A	
Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A  Inhalation solution Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single	
Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)	
Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate dose without an AeroChamber Plus® Floring Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)	
Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate dose without an AeroChamber Plus® Flo Investigational medicinal product name Investigational medicinal product code	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer	
Investigational medicinal product name  Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Two inhalations of Mometasone Furoate dose without an AeroChamber Plus® Floring Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer  SCH 418131, MK-0877A  Inhalation solution  Inhalation use  /Formoterol Fumarate MDI 50/5 mcg administered as a single ow-Vu® Anti-Static Valved Holding Chamber (spacer)  Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator)	

Routes of administration	Inhalation use
Dosage and administration details:	
•	Formoterol Fumarate MDI 50/5 mcg administered as a single /u® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administe Anti-Static Valved Holding Chamber (spa	ered as a single dose without an AeroChamber Plus® Flow-Vu®cer)
Arm title	Treatment Sequence 6
Arm description:	
Treatment Period 1: MF/F MDI with space Period 3: MF/F MDI without spacer, Treatment	er, Treatment Period 2: Placebo MDI without spacer, Treatment tment Period 4: F DPI
Arm type	Experimental
Investigational medicinal product name	Formoterol Fumarate DPI
Investigational medicinal product code	
Other name	SCH 045571, MK-5571, Foradil® Aerolizer®
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of Formoterol Fumarate	DPI 10 mcg administered as a single dose
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) without spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single w-Vu® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Mometasone Furoate/Formoterol Fumarate MDI (ex-actuator) with spacer
Investigational medicinal product code	
Other name	SCH 418131, MK-0877A
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
	Formoterol Fumarate MDI 50/5 mcg administered as a single (u® Anti-Static Valved Holding Chamber (spacer)
Investigational medicinal product name	Placebo MDI without spacer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use
Dosage and administration details:	
Two inhalations of placebo MDI administe	ered as a single dose without an AeroChamber Plus® Flow-Vu®

Anti-Static Valved Holding Chamber (spacer)

[4] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was an evaluator-blind study. The investigator, clinical study staff and personnel performing the assessments and data analysis were to remain blinded to the identity of the study medication and treatment sequence. The Third-Party Dispenser was the only one at the site who knew

the treatment assignment of each subject.

Number of subjects in period 4	Treatment Sequence 1	Treatment Sequence 2	Treatment Sequence 3
Started	14	14	14
Completed	14	14	14

Number of subjects in period 4	Treatment Sequence 4	Treatment Sequence 5	Treatment Sequence 6
Started	15	15	15
Completed	15	15	15

### **Baseline characteristics**

Reporting groups		
Reporting group title	Treatment Period 1 (1 dose)	
Reporting group description:		
All Randomized Participants		

Reporting group values	Treatment Period 1 (1 dose)	Total	
Number of subjects	92	92	
Age, Customized			
Units: participants			
5-7 years	17	17	
8-11 years	75	75	
Age continuous			
Units:			
	9.1		
	± 1.7	-	
Gender, Male/Female			
Units: participants			
Female	35	35	
Male	57	57	

### **End points**

End points reporting grou	ıps
Reporting group title	Treatment Sequence 1
Reporting group description:	
	etered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometason MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer, der Inhaler (DPI)
Reporting group title	Treatment Sequence 2
Reporting group description:	
	atment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F riod 4: Placebo MDI with spacer
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Period 1: MF/F MDI with spacer, Treatment Per	without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo riod 4: MF/F MDI with spacer
Reporting group title	Treatment Sequence 4
Reporting group description:	
	OI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatmen od 4: MF/F MDI without spacer
Reporting group title	Treatment Sequence 5
Reporting group description:	
	without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F riod 4: Placebo MDI without spacer
Reporting group title	Treatment Sequence 6
Reporting group description:	
	with spacer, Treatment Period 2: Placebo MDI without spacer, Treatmer Icer, Treatment Period 4: F DPI
Reporting group title	Treatment Sequence 1
Reporting group description:	
Freatment Period 1: Placebo ME Period 3: MF/F MDI with spacer	DI with spacer, Treatment Period 2: MF/F MDI without spacer, Treatmer , Treatment Period 4: F DPI
Reporting group title	Treatment Sequence 2
Reporting group description:	
	atment Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F riod 4: Placebo MDI with spacer
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Period 1: MF/F MDI with spacer, Treatment Per	without spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo riod 4: MF/F MDI with spacer
Reporting group title	Treatment Sequence 4
Reporting group description:	
	DI without spacer, Treatment Period 2: MF/F MDI with spacer, Treatmer od 4: MF/F MDI without spacer
Reporting group title	Treatment Sequence 5
Reporting group description:	
	without spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F riod 4: Placebo MDI without spacer
Reporting group title	Treatment Sequence 6
Reporting group description:	
	with spacer, Treatment Period 2: Placebo MDI without spacer, Treatmer icer, Treatment Period 4: F DPI
Reporting group title	Treatment Sequence 1
Reporting group description:	
Frontmont Doried 1, Discobe Ma	etered Dose Inhaler (MDI) with spacer, Treatment Period 2: Mometason

Treatment Period 4: F Dry Powder I	nhaler (DPI)
Reporting group title	Treatment Sequence 2
Reporting group description:	·
Treatment Period 1: F DPI, Treatment MDI with spacer, Treatment Period	ent Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F 4: Placebo MDI with spacer
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Period 1: MF/F MDI without MDI with spacer, Treatment Period	out spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo 4: MF/F MDI with spacer
Reporting group title	Treatment Sequence 4
Reporting group description:	
Treatment Period 1: Placebo MDI wi Period 3: F DPI, Treatment Period 4	ithout spacer, Treatment Period 2: MF/F MDI with spacer, Treatment : MF/F MDI without spacer
Reporting group title	Treatment Sequence 5
Reporting group description:	
Treatment Period 1: MF/F MDI with MDI with spacer, Treatment Period	out spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F 4: Placebo MDI without spacer
Reporting group title	Treatment Sequence 6
Reporting group description:	
Treatment Period 1: MF/F MDI with Period 3: MF/F MDI without spacer,	spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Treatment Period 4: F DPI
Reporting group title	Treatment Sequence 1
Reporting group description:	
Treatment Period 1: Placebo MDI wi Period 3: MF/F MDI with spacer, Tre	ith spacer, Treatment Period 2: MF/F MDI without spacer, Treatment eatment Period 4: F DPI
Reporting group title	Treatment Sequence 2
Reporting group description:	
Treatment Period 1: F DPI, Treatme MDI with spacer, Treatment Period	ent Period 2: MF/F MDI without spacer, Treatment Period 3: MF/F 4: Placebo MDI with spacer
Reporting group title	Treatment Sequence 3
Reporting group description:	
Treatment Period 1: MF/F MDI without MDI with spacer, Treatment Period	out spacer, Treatment Period 2: F DPI, Treatment Period 3: Placebo 4: MF/F MDI with spacer
Reporting group title	Treatment Sequence 4
Reporting group description:	
Treatment Period 1: Placebo MDI wi Period 3: F DPI, Treatment Period 4	ithout spacer, Treatment Period 2: MF/F MDI with spacer, Treatment : MF/F MDI without spacer
Reporting group title	Treatment Sequence 5
Reporting group description:	
Treatment Period 1: MF/F MDI without MDI with spacer, Treatment Period	out spacer, Treatment Period 2: F DPI, Treatment Period 3: MF/F 4: Placebo MDI without spacer
Reporting group title	Treatment Sequence 6
Reporting group description:	
Treatment Period 1: MF/F MDI with Period 3: MF/F MDI without spacer,	spacer, Treatment Period 2: Placebo MDI without spacer, Treatment Treatment Period 4: F DPI
Subject analysis set title	MF/F MDI with spacer
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants receiving a single dose	of MF/F MDI 100/10 mcg with a spacer
Subject analysis set title	MF/F MDI without spacer
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants receiving a single dose	of MF/F MDI 100/10 mcg without a spacer
Subject analysis set title	F DPI
Subject analysis set type	Full analysis
	•

EU-CTR publication date: 16 February 2016

Furoate/Formoterol Fumarate (MF/F) MDI without spacer, Treatment Period 3: MF/F MDI with spacer,

Subject analysis set description:

Participants receiving a single dose of F DPI 20 mcg

Subject analysis set title	Placebo MDI with or without spacer
Subject analysis set type	Full analysis
Subject analysis set description:	

Subject analysis set description:

Participants receiving a single dose of Placebo MDI with or without a spacer

## Primary: Area Under the Curve From 0-12 hours (AUC[0-12h]) of the Change From baseline in Forced Expiratory Volume in 1 Second (FEV1) After a Single Dose of MF/F MDI With Spacer Compared to Placebo MDI Combined With or Without Spacer

End point title	Area Under the Curve From 0-12 hours (AUC[0-12h]) of the
	Change From baseline in Forced Expiratory Volume in 1 Second
	(FEV1) After a Single Dose of MF/F MDI With Spacer Compared
	to Placebo MDI Combined With or Without Spacer

#### End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Primary
End point timeframe:	
Up to 12 hours postdose	

End point values	MF/F MDI with spacer	Placebo MDI with or without spacer	
Subject group type	Subject analysis set	Subject analysis set	
Number of subjects analysed	79	79	
Units: Liters			
least squares mean (standard error)	0.115 (± 0.016)	-0.009 (± 0.016)	

#### Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose
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#### Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI with spacer and Placebo MDI combined with or without spacer. Analysis was performed using an analysis of covariance (ANCOVA) model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.124
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.094
upper limit	0.154

## Secondary: AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose MF/F MDI Without Spacer Compared to Placebo MDI Combined With or Without Spacer

AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose MF/F MDI Without Spacer Compared to Placebo MDI
Combined With or Without Spacer

#### End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary
End point timeframe:	
Up to 12 hours postdose	

End point values	Placebo MDI with or without spacer	MF/F MDI without spacer	
Subject group type	Subject analysis set	Subject analysis set	
Number of subjects analysed	79	79	
Units: Liters			
least squares mean (standard error)	-0.009 (± 0.016)	0.093 (± 0.016)	

#### Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

#### Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI without spacer and Placebo MDI combined with or without spacer. Analysis was performed using an ANCOVA model extracting the effects due to treatment,

sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

MF/F MDI without spacer v Placebo MDI with or without spacer
158
Pre-specified
superiority
< 0.001
ANCOVA
Mean difference (final values)
0.102
95 %
2-sided
0.073
0.131

## Secondary: AUC(0-12h) of the Change From Baseline in FEV1 After a Single Dose of MF/F MDI With Spacer Compared to MF/F MDI Without Spacer

End point title	AUC(0-12h) of the Change From Baseline in FEV1 After a Single
	Dose of MF/F MDI With Spacer Compared to MF/F MDI Without
	Spacer

#### End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary
End point timeframe:	
Up to 12 hours postdose	

End point values	MF/F MDI with spacer	MF/F MDI without spacer	
Subject group type	Subject analysis set	Subject analysis set	
Number of subjects analysed	79	79	
Units: Liters			
least squares mean (standard error)	0.115 (± 0.016)	0.093 (± 0.016)	

#### Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI with spacer and MF/F MDI without spacer. Analysis was

performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

MF/F MDI with spacer v MF/F MDI without spacer
158
Pre-specified
superiority
= 0.144
ANCOVA
Mean difference (final values)
0.022
95 %
2-sided
-0.008
0.052

## Secondary: AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of MF/F With Spacer Compared to F DPI

End point title	AUC (0-12h) of the Change From Baseline in FEV1 After a
	Single Dose of MF/F With Spacer Compared to F DPI

#### End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, space and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary
End point timeframe:	
Up to 12 hours postdose	

End point values	MF/F MDI with spacer	F DPI	
Subject group type	Subject analysis set	Subject analysis set	
Number of subjects analysed	79	79	
Units: Liters			
least squares mean (standard error)	0.115 (± 0.016)	0.097 (± 0.016)	

#### Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

EU-CTR publication date: 16 February 2016

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI with spacer and F DPI.

Analysis was performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI with spacer v F DPI
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.229
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.018
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.012
upper limit	0.048

## Secondary: AUC (0-12h) of the Change from Baseline in FEV1 After a Single Dose of MF/F Without Spacer Compared to F DPI

Single Dose of MF/F Without Spacer Compared to F DPI		AUC (0-12h) of the Change from Baseline in FEV1 After a Single Dose of MF/F Without Spacer Compared to F DPI
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#### End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, space and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary
End point timeframe:	
Up to 12 hours postdose	

End point values	MF/F MDI without spacer	F DPI	
Subject group type	Subject analysis set	Subject analysis set	
Number of subjects analysed	79	79	
Units: Liters			
least squares mean (standard error)	0.093 (± 0.016)	0.097 (± 0.016)	

#### Statistical analyses

Statistical analysis title	AUC(0-12h) chg from BL in FEV1 after single dose

Statistical analysis description:

Pairwise Treatment Comparison of MF/F MDI without spacer and F DPI.

Analysis was performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	MF/F MDI without spacer v F DPI
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.79
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.033
upper limit	0.025

## Secondary: AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of F DPI Compared to Placebo MDI Combined With or Without Spacer

·	AUC (0-12h) of the Change From Baseline in FEV1 After a Single Dose of F DPI Compared to Placebo MDI Combined With or Without Spacer
	o. manda opada.

#### End point description:

The AUC was standardized to liters by dividing the length of time for which measurements of FEV1 were included in the calculation of the AUC. Baseline was defined as the average of 2 pre-dose FEV1 measurements (taken 30 minutes before and immediately before dosing), which was subtracted from each of the serial FEV1 measurements over the 12-hour period. The AUC was calculated based on these changes from the baseline evaluations using the trapezoidal rule. The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, space and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary
End point timeframe:	
Up to 12 hours postdose	

End point values	Placebo MDI with or without spacer	F DPI	
		Subject analysis set	

#### Statistical analysis title AUC(0-12h) chg from BL in FEV1 after single dose

#### Statistical analysis description:

Pairwise Treatment Comparison of F DPI and Placebo MDI combined with or without spacer. Analysis was performed using an ANCOVA model extracting the effects due to treatment, sequence, subject (random effect nested within sequence), period, age groups (5 to 7 years and 8 to 11 years) and Baseline FEV1 as a covariate.

Comparison groups	F DPI v Placebo MDI with or without spacer
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.106
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.077
upper limit	0.135

#### Secondary: Change from Baseline in Forced Vital Capacity (FVC) After a Single Dose of MF/F MDI With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours **Postdose**

End point title	Change from Baseline in Forced Vital Capacity (FVC) After a
	Single Dose of MF/F MDI With Spacer, MF/F MDI Without
	Spacer, F DPI or Placebo MDI Combined With or Without
	Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours Postdose

#### End point description:

Baseline was defined as the average of 2 predose FVC measurements (taken 30 minutes and immediately before dosing). The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary	
End point timeframe:		
Baseline and 5 and 30 minutes, 1, 2, 4, 8 and 12 hours postdose		

End point values	MF/F MDI with spacer	Placebo MDI with or without spacer	MF/F MDI without spacer	F DPI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Liters				
least squares mean (standard error)				
Baseline (n=79,79,79,79)	1.914 (± 0.061)	1.913 (± 0.061)	1.931 (± 0.061)	1.928 (± 0.061)
5 minutes postdose (n=79,79,79,79)	0.028 (± 0.012)	0.018 (± 0.012)	0.005 (± 0.012)	0.032 (± 0.012)

30 minutes postdose (n=79,79,79,79)	0.037 (± 0.013)	0.009 (± 0.013)	0.02 (± 0.013)	0.017 (± 0.013)
1 hour postdose (n=79,79,79,79)	0.048 (±	-0.003 (±	0.027 (±	0.022 (±
	0.015)	0.014)	0.014)	0.014)
2 hours postdose (n=79,79,79,79)	0.023 (±	0.015 (±	0.026 (±	0.047 (±
	0.015)	0.015)	0.015)	0.015)
4 hours postdose (n=79,79,79,79)	0.031 (±	-0.006 (±	0.018 (±	0.008 (±
	0.015)	0.015)	0.015)	0.015)
8 hours postdose (n=79,79,79,79)	-0.001 (±	-0.006 (±	0.007 (±	-0.013 (±
	0.016)	0.015)	0.015)	0.015)
12 hours postdose (n=78,79,78,79)	-0.001 (±	-0.012 (±	-0.022 (±	-0.014 (±
	0.017)	0.016)	0.016)	0.016)

#### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in FEV1 After a Single Dose of MF/F MDI With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4, 8 and 12 Hours Postdose

End point title	Change from Baseline in FEV1 After a Single Dose of MF/F MDI
	With Spacer, MF/F MDI Without Spacer, F DPI or Placebo MDI
	Combined With or Without Spacer at 5 and 30 Minutes, 1, 2, 4,
	8 and 12 Hours Postdose

#### End point description:

Baseline was defined as the average of 2 predose measurements (taken 30 minutes and immediately before dosing). The analysis population for this endpoint included all participants who received each assigned single-dose treatment, performed at least the 0- and 2-hour spirometry evaluations and met the following criteria: did not use any prohibited concomitant medications; demonstrated satisfactory use of inhaler, spacer and spirometry maneuvers; and used >80% of prescribed MF DPI across the entire study treatment.

End point type	Secondary	
End point timeframe:		
Baseline and 5 and 30 minutes, 1, 2, 4, 8 and 12 hours postdose		

End point values	MF/F MDI with spacer	Placebo MDI with or without spacer	MF/F MDI without spacer	F DPI
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Liters				
least squares mean (standard error)				
Baseline (n=79,79,79,79)	1.554 (± 0.049)	1.547 (± 0.049)	1.563 (± 0.049)	1.57 (± 0.049)
5 minutes postdose (n=79,79,79,79)	0.111 (± 0.014)	-0.001 (± 0.014)	0.068 (± 0.013)	0.105 (± 0.013)
30 minutes postdose (n=79,79,79,79)	0.131 (± 0.017)	0.006 (± 0.016)	0.099 (± 0.016)	0.117 (± 0.016)
1 hour postdose (n=79,79,79,79)	0.159 (± 0.017)	0.007 (± 0.016)	0.131 (± 0.016)	0.136 (± 0.016)
2 hours postdose (n=79,79,79,79)	0.136 (± 0.018)	0.019 (± 0.018)	0.126 (± 0.018)	0.135 (± 0.018)

4 hours postdose (n=79,79,79,79)	0.136 (±	0.005 (±	0.115 (±	0.118 (±
	0.018)	0.018)	0.018)	0.018)
8 hours postdose (n=79,79,79,79)	0.108 (±	-0.012 (±	0.093 (±	0.087 (±
	0.018)	0.018)	0.018)	0.017)
12 hours postdose (n=78,79,78,79)	0.092 (±	-0.033 (±	0.046 (±	0.059 (±
	0.019)	0.019)	0.018)	0.018)

### Statistical analyses

No statistical analyses for this end point

#### **Adverse events**

#### Adverse events information[1]

Timeframe for reporting adverse events:

Adverse event data were collected for up to 30 days after last dose of study drug (up to a total of 90 days)

Adverse event reporting additional description:

The Safety Population consisted of all randomized participants who received at least one dose of the study drug.

Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

#### Reporting groups

Reporting group title	MF/F MDI with spacer

Reporting group description:

Participants receiving a single dose of MF/F MDI 100/10 mcg with a spacer

Reporting group title	F DPI
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Reporting group description:

Participants receiving a single dose of F DPI 20 mcg

Reporting group title	Placebo MDI with or without spacer
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Reporting group description:

Participants receiving a single dose of Placebo MDI with or without a spacer

Reporting group title	MF/F MDI without spacer
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Reporting group description:

Participants receiving a single dose of MF/F MDI 100/10 mcg without a spacer

Serious adverse events	MF/F MDI with spacer	F DPI	Placebo MDI with or without spacer
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 90 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	MF/F MDI without spacer	
Total subjects affected by serious adverse events		
subjects affected / exposed	0 / 91 (0.00%)	
number of deaths (all causes)	0	
number of deaths resulting from adverse events		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	MF/F MDI with spacer	F DPI	Placebo MDI with or without spacer
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)	0 / 90 (0.00%)	0 / 90 (0.00%)

Non-serious adverse events	MF/F MDI without spacer	
Total subjects affected by non-serious adverse events		
subjects affected / exposed	0 / 91 (0.00%)	

#### Notes:

<sup>[1]</sup> - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: In this study, no non-serious adverse events reached the 5% frequency threshold for reporting.

#### **More information**

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2010	Amendment 1: Changes to Inclusion Criterion 14: text added to be consistent with other references in protocol: Subject must be able to demonstrate his/her ability to perform reproducible expiratory maneuvers (including PEF), following the principles of the ATS/ERS guidelines. Text also modified in following procedures: 7.Review of prior medications, including washout times, with subject. Record of prior medication taken by subject within 30 days, or longer, if applicable as per washout requirements, before starting trial to be obtained; 14.Venous blood and urine samples specified in Table 8 (protocol) to be analyzed and reported by central laboratory using standard procedures. Urine pregnancy test for female subjects of childbearing potential to be taken at Screening Visit and Visit 5 or Discontinuation Visit; must be negative for subject to be considered for eligibility. If subject is menstruating at time of urine collection, it should be noted in the source and eCRF comment module. Female subjects who begin menses after Screening Visit will have urine pregnancy test at next scheduled visit. Subjects with positive test will be discontinued; 16.Subjects to refrain from using SABA for 6 hours prior to start of spirometry unless FEV1 falls below stability limit. Spirometry to be performed following principles of ATS/ERS guidelines; should be performed with subject sitting, using a chair with arms and without wheels; if necessary, undertake testing with subject standing or in another position and note on spirometry report; position should be demonstrated within 30 minutes of bronchodilator administration. If subject does not meet reversibility at Visit 1, three repeat assessments can be performed during Run-in Period, prior to Baseline Visit; 18.e-Diary/PEF meter will collect and save relevant expiratory flow-volume parameters, use of rescue medication, and dosing information.
17 December 2010	Amendment 2: The only change the protocol was reinserting missing pages in Appendix 8.

Notes:

### **Interruptions (globally)**

Were there any global interruptions to the trial? No

#### **Limitations and caveats**

None reported