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Trial record **1 of 1** for: CQAB149B2348

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Exacerbation Study (INVIGORATE)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00845728

First received: February 15, 2009
Last updated: September 16, 2013
Last verified: September 2013
History of Changes

Full Text View | Tabular View | **Study Results** | Disclaimer | How to Read a Study Record

Results First Received: July 3, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Chronic Obstructive Pulmonary Disease
Interventions:	Drug: Indacaterol 150 µg Drug: Tiotropium

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
3,444 patients were randomized, but only 3,439 received treatment as 5 patients were mis-randomized.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Indacaterol	Indacaterol 150 µg o.d., delivered via SDDPI o.d. plus placebo to tiotropium o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®)
Tiotropium	Tiotropium 18 µg o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®) plus placebo to indacaterol o.d. delivered via SDDPI

Participant Flow: Overall Study

	Indacaterol	Tiotropium
STARTED	1723	1721
Exposed	1721	1718
COMPLETED	1337	1379
NOT COMPLETED	386	342
Abnormal laboratory value (s)	2	2
Patient's inability to use the device	4	6

Abnormal test procedure result (s)	**7**	**2**
Lost to Follow-up	**22**	**13**
Death	**24**	**26**
Administrative Problems	**34**	**26**
Protocol Violation	**36**	**24**
Lack of Efficacy	**51**	**39**
Adverse Event	**101**	**96**
Withdrawal by Subject	**105**	**108**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Indacaterol	Indacaterol 150 µg o.d., delivered via SDDPI o.d. plus placebo to tiotropium o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®)
Tiotropium	Tiotropium 18 µg o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®) plus placebo to indacaterol o.d. delivered via SDDPI
Total	Total of all reporting groups

Baseline Measures

	Indacaterol	Tiotropium	Total
Number of Participants [units: participants]	**1721**	**1718**	**3439**
Age, Customized [units: Participants]			
<65 years	**929**	**909**	**1838**
≥ 65 years	**792**	**809**	**1601**
Gender [units: Participants]			
Female	**377**	**405**	**782**
Male	**1344**	**1313**	**2657**

Outcome Measures

Hide All Outcome Measures

1. Primary: Trough Forced Expiratory Volume in 1 Second (FEV1). [Time Frame: 12 weeks]

Measure Type	Primary
Measure Title	Trough Forced Expiratory Volume in 1 Second (FEV1).
Measure Description	The primary objective of the study was to demonstrate the non-inferiority of indacaterol vs. tiotropium with respect to 24 hour post dose (trough) FEV1 after 12 weeks of treatment in patients with severe COPD. Trough FEV1 was defined as the average of the 23 hours 10 min and the 23 hours 45 min post dose values. Trough FEV1 was analyzed using a mixed model for the PPS-S. The model contained treatment as a fixed effect with the baseline FEV1, FEV1 prior to inhalation and FEV1 15 min post-inhalation of salbutamol/albuterol (components of SABA reversibility at Visit 2), FEV1 prior to inhalation and FEV1 60 min post-inhalation of ipratropium (components of anti-cholinergic reversibility at Visit 3) as covariates. Smoking history (current or ex-smoker) was included as a factor in the model.

Time Frame	12 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per-Protocol Set for Spirometry (PPS-S) This set included Full Analysis Set (FAS) patients without any major protocol deviations or non-protocol deviation criteria that could affect the respective analysis of efficacy.

Reporting Groups

	Description
Indacaterol	Indacaterol 150 µg o.d., delivered via SDDPI o.d. plus placebo to tiotropium o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®)
Tiotropium	Tiotropium 18 µg o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®) plus placebo to indacaterol o.d. delivered via SDDPI

Measured Values

	Indacaterol	Tiotropium
Number of Participants Analyzed [units: participants]	**1450**	**1467**
Trough Forced Expiratory Volume in 1 Second (FEV1). [units: Liters] Least Squares Mean (Standard Error)	**1.134 (0.0008)**	**1.145 (0.0008)**

No statistical analysis provided for Trough Forced Expiratory Volume in 1 Second (FEV1).

2. Secondary: Rate of COPD Exacerbations [Time Frame: 52 weeks]

Measure Type	Secondary
Measure Title	Rate of COPD Exacerbations
Measure Description	COPD exacerbations were defined as :Worsening of 2 or more major symptoms for at least 2 consecutive days: dyspnea; sputum volume; suputum purulence AND requiring treatment with systemic corticosteroids and/or antibiotics OR Worsening of any 1 major symptom together with any 1 of the following minor symptoms for at least 2 consecutive days: Sore throat; colds; fever without other cause; increased cough; increase wheeze AND requiring treatment with systemic glucocorticosteroids and/or antibiotics. The rate was analyzed using a linear model assuming a negative binomial distribution for the PPS-E. The time at risk for a patient was defined as the length of time the patient was in the study and the log(length of time in the study) was used as the offset variable in the model.
Time Frame	52 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per-Protocol Set for Exacerbations (PPS-E). This set included Full Analysis Set (FAS) patients without any major protocol deviations or non-protocol deviation criteria that could affect the respective analysis of efficacy.

Reporting Groups

	Description
Indacaterol	Indacaterol 150 µg o.d., delivered via SDDPI o.d. plus placebo to tiotropium o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®)
Tiotropium	Tiotropium 18 µg o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®) plus placebo to indacaterol o.d. delivered via SDDPI

Measured Values

	Indacaterol	**Tiotropium**
Number of Participants Analyzed [units: participants]	**1675**	**1675**

Rate of COPD Exacerbations [units: Exacerbations per patient per year]	**0.79**	**0.61**

No statistical analysis provided for Rate of COPD Exacerbations

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
IndIndacaterol	Indacaterol 150 µg o.d., delivered via SDDPI o.d. plus placebo to tiotropium o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®)
Tiotropium	Tiotropium 18 µg o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®) plus placebo to indacaterol o.d. delivered via SDDPI

Serious Adverse Events

	IndIndacaterol	Tiotropium
Total, serious adverse events		
# participants affected / at risk	**263/1721 (15.28%)**	**255/1718 (14.84%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**3/1718 (0.17%)**
Iron deficiency anaemia † 1		

# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Leukopenia † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Cardiac disorders		
Acute coronary syndrome † [1]		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Acute myocardial infarction † [1]		
# participants affected / at risk	3/1721 (0.17%)	2/1718 (0.12%)
Angina pectoris † [1]		
# participants affected / at risk	5/1721 (0.29%)	5/1718 (0.29%)
Angina unstable † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Aortic valve calcification † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Arrhythmia † [1]		
# participants affected / at risk	3/1721 (0.17%)	1/1718 (0.06%)
Arrhythmia supraventricular † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Arteriosclerosis coronary artery † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Atrial fibrillation † [1]		
# participants affected / at risk	3/1721 (0.17%)	4/1718 (0.23%)
Atrial flutter † [1]		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
Atrioventricular block † [1]		

# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Atrioventricular block first degree † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Bradycardia † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Bundle branch block left † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Cardiac arrest † 1		
# participants affected / at risk	**3/1721 (0.17%)**	**2/1718 (0.12%)**
Cardiac failure † 1		
# participants affected / at risk	**3/1721 (0.17%)**	**5/1718 (0.29%)**
Cardiac failure chronic † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Cardiac failure congestive † 1		
# participants affected / at risk	**3/1721 (0.17%)**	**1/1718 (0.06%)**
Cardio-respiratory arrest † 1		
# participants affected / at risk	**3/1721 (0.17%)**	**2/1718 (0.12%)**
Cardiomegaly † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Cardiomyopathy † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Cardiopulmonary failure † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Congestive cardiomyopathy † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**

Cor pulmonale † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Coronary artery disease † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**3/1718 (0.17%)**
Cyanosis † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Diastolic dysfunction † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Ischaemic cardiomyopathy † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Left ventricular hypertrophy † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Mitral valve incompetence † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Myocardial infarction † [1]		
# participants affected / at risk	**4/1721 (0.23%)**	**8/1718 (0.47%)**
Myocardial ischaemia † [1]		
# participants affected / at risk	**6/1721 (0.35%)**	**4/1718 (0.23%)**
Palpitations † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Right ventricular failure † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Sinus bradycardia † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Supraventricular extrasystoles † [1]		

# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Tachyarrhythmia † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Ear and labyrinth disorders		
Hypoacusis † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Vertigo † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Endocrine disorders		
Goitre † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Eye disorders		
Angle closure glaucoma † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Cataract † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Maculopathy † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Retinal vein occlusion † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Gastrointestinal disorders		
Abdominal hernia † 1		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Abdominal pain † 1		

# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Abdominal pain upper † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Acute abdomen † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Ascites † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Colitis † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Colitis ulcerative † 1		
# participants affected / at risk	0/1721 (0.00%)	3/1718 (0.17%)
Colonic polyp † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Constipation † 1		
# participants affected / at risk	1/1721 (0.06%)	3/1718 (0.17%)
Diarrhoea † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Diverticulum † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Duodenal fistula † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Duodenitis † 1		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Enteritis † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)

Gastric ulcer † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Gastritis † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Gastrooesophageal reflux disease † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Haematemesis † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Ileus † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Inguinal hernia † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Intestinal ischaemia † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Intestinal obstruction † [1]		
# participants affected / at risk	**3/1721 (0.17%)**	**0/1718 (0.00%)**
Mallory-Weiss syndrome † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Melaena † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Nausea † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**0/1718 (0.00%)**
Oesophagitis † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Pancreatitis † [1]		

# participants affected / at risk	0/1721 (0.00%)	3/1718 (0.17%)
Pancreatitis acute † 1		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Regurgitation † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Sigmoiditis † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Small intestinal obstruction † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Thrombosis mesenteric vessel † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Umbilical hernia † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Upper gastrointestinal haemorrhage † 1		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
General disorders		
Chills † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Death † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Device dislocation † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Drug ineffective † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Malaise † 1		

# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Multi-organ failure † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Non-cardiac chest pain † 1		
# participants affected / at risk	4/1721 (0.23%)	1/1718 (0.06%)
Oedema due to cardiac disease † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Oedema peripheral † 1		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
Pyrexia † 1		
# participants affected / at risk	3/1721 (0.17%)	1/1718 (0.06%)
Soft tissue inflammation † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Sudden cardiac death † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Sudden death † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Hepatobiliary disorders		
Bile duct stone † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Cholangitis acute † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Cholecystitis † 1		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Cholelithiasis † 1		

# participants affected / at risk	1/1721 (0.06%)	2/1718 (0.12%)
Gallbladder fistula † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Hepatic function abnormal † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Hyperbilirubinaemia † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Jaundice † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Immune system disorders		
Drug hypersensitivity † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Infections and infestations		
Anal abscess † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Appendicitis perforated † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Bronchitis † 1		
# participants affected / at risk	3/1721 (0.17%)	2/1718 (0.12%)
Bronchitis bacterial † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Bronchopneumonia † 1		
# participants affected / at risk	2/1721 (0.12%)	3/1718 (0.17%)
Clostridial infection † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)

Diverticulitis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**2/1718 (0.12%)**
Gastroenteritis † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
H1N1 influenza † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Helicobacter infection † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Herpes zoster † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**4/1718 (0.23%)**
Influenza † 1		
# participants affected / at risk	**4/1721 (0.23%)**	**2/1718 (0.12%)**
Intervertebral discitis † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Lobar pneumonia † 1		
# participants affected / at risk	**4/1721 (0.23%)**	**4/1718 (0.23%)**
Lower respiratory tract infection † 1		
# participants affected / at risk	**28/1721 (1.63%)**	**18/1718 (1.05%)**
Lower respiratory tract infection bacterial † 1		
# participants affected / at risk	**4/1721 (0.23%)**	**2/1718 (0.12%)**
Lower respiratory tract infection viral † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Lung abscess † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Lung infection † 1		

# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Meningitis † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Meningitis viral † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Nasopharyngitis † [1]		
# participants affected / at risk	3/1721 (0.17%)	3/1718 (0.17%)
Oral candidiasis † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Pneumococcal sepsis † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Pneumonia † [1]		
# participants affected / at risk	29/1721 (1.69%)	24/1718 (1.40%)
Pneumonia bacterial † [1]		
# participants affected / at risk	1/1721 (0.06%)	2/1718 (0.12%)
Pneumonia pneumococcal † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Pneumonia staphylococcal † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Pseudomonas infection † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Pulmonary tuberculosis † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Respiratory tract infection bacterial † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)

Respiratory tract infection viral † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Sepsis † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Septic shock † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**3/1718 (0.17%)**
Sinusitis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Testicular abscess † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Tracheobronchitis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**3/1721 (0.17%)**	**2/1718 (0.12%)**
Upper respiratory tract infection bacterial † 1		
# participants affected / at risk	**18/1721 (1.05%)**	**16/1718 (0.93%)**
Urinary tract infection † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**2/1718 (0.12%)**
Urosepsis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Viral sepsis † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Viral upper respiratory tract infection † 1		
# participants affected / at risk	**12/1721 (0.70%)**	**11/1718 (0.64%)**
Injury, poisoning and procedural complications		

Ankle fracture † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Concussion † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Contusion † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Fall † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**1/1718 (0.06%)**
Femoral neck fracture † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**2/1718 (0.12%)**
Femur fracture † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Hip fracture † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Penetrating abdominal trauma † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Post procedural fistula † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Rib fracture † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**1/1718 (0.06%)**
Tibia fracture † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Traumatic shock † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Investigations		

Arteriogram coronary † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
C-reactive protein increased † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Prostatic specific antigen increased † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Metabolism and nutrition disorders		
Decreased appetite † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Diabetes mellitus † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Diabetes mellitus inadequate control † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Hyperkalaemia † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**0/1718 (0.00%)**
Hyponatraemia † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Musculoskeletal and connective tissue disorders		
Axillary mass † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Back pain † [1]		
# participants affected / at risk	**4/1721 (0.23%)**	**0/1718 (0.00%)**
Cervical spinal stenosis † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Exostosis † [1]		

# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Intervertebral disc degeneration † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Intervertebral disc disorder † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Intervertebral disc protrusion † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Musculoskeletal chest pain † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Musculoskeletal pain † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Myalgia † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Neck pain † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Osteonecrosis † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Rotator cuff syndrome † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Spinal column stenosis † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Spinal osteoarthritis † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Benign neoplasm of prostate † 1		

# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Bladder cancer † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Bladder papilloma † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Breast cancer † 1		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Bronchial carcinoma † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Colon adenoma † 1		
# participants affected / at risk	2/1721 (0.12%)	0/1718 (0.00%)
Colon cancer † 1		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
Colon neoplasm † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Gallbladder cancer † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Gastric cancer † 1		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Glioblastoma † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Lung adenocarcinoma † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Lung cancer metastatic † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)

Lung neoplasm † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Lung neoplasm malignant † 1		
# participants affected / at risk	**4/1721 (0.23%)**	**5/1718 (0.29%)**
Metastases to central nervous system † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Metastases to peritoneum † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Myelofibrosis † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Neoplasm malignant † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Neoplasm prostate † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Ovarian cancer † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Pancreatic carcinoma † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Prostate cancer † 1		
# participants affected / at risk	**3/1721 (0.17%)**	**1/1718 (0.06%)**
Prostatic adenoma † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Rectal cancer † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Rectal neoplasm † 1		

# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Renal cancer † [1]		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Salivary gland adenoma † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Squamous cell carcinoma of skin † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Nervous system disorders		
Amyotrophic lateral sclerosis † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Brain injury † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Cerebral haemorrhage † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Cerebral infarction † [1]		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
Cerebral ischaemia † [1]		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Cerebral thrombosis † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Cerebrovascular accident † [1]		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
Coma † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Depressed level of consciousness † [1]		

# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Dizziness † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Grand mal convulsion † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Haemorrhage intracranial † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Headache † 1		
# participants affected / at risk	2/1721 (0.12%)	0/1718 (0.00%)
Hypoglycaemic coma † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Hypoxic-ischaemic encephalopathy † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Intracranial aneurysm † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Ischaemic stroke † 1		
# participants affected / at risk	2/1721 (0.12%)	0/1718 (0.00%)
Lacunar infarction † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Memory impairment † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Peripheral sensorimotor neuropathy † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Peripheral sensory neuropathy † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)

Presyncope † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Sensory loss † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Spinal cord compression † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Syncope † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Transient ischaemic attack † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**4/1718 (0.23%)**
Vascular encephalopathy † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Psychiatric disorders		
Anxiety † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Completed suicide † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**2/1718 (0.12%)**
Confusional state † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Depression † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Renal and urinary disorders		
Bladder neck obstruction † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Haematuria † [1]		

# participants affected / at risk	2/1721 (0.12%)	0/1718 (0.00%)
Nephrotic syndrome † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Renal failure † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Renal failure acute † 1		
# participants affected / at risk	3/1721 (0.17%)	0/1718 (0.00%)
Urethral stenosis † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Urinary retention † 1		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia † 1		
# participants affected / at risk	2/1721 (0.12%)	3/1718 (0.17%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory distress syndrome † 1		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Acute respiratory failure † 1		
# participants affected / at risk	4/1721 (0.23%)	2/1718 (0.12%)
Apnoea † 1		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Chronic obstructive pulmonary disease † 1		
# participants affected / at risk	147/1721 (8.54%)	121/1718 (7.04%)
Cough † 1		

# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Dyspnoea † [1]		
# participants affected / at risk	12/1721 (0.70%)	4/1718 (0.23%)
Haemoptysis † [1]		
# participants affected / at risk	1/1721 (0.06%)	1/1718 (0.06%)
Hydrothorax † [1]		
# participants affected / at risk	0/1721 (0.00%)	2/1718 (0.12%)
Hypercapnia † [1]		
# participants affected / at risk	2/1721 (0.12%)	1/1718 (0.06%)
Hypoxia † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Interstitial lung disease † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Laryngeal oedema † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Lung disorder † [1]		
# participants affected / at risk	0/1721 (0.00%)	1/1718 (0.06%)
Lung infiltration † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Oropharyngeal pain † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Pleural effusion † [1]		
# participants affected / at risk	1/1721 (0.06%)	0/1718 (0.00%)
Pleurisy † [1]		
# participants affected / at risk	2/1721 (0.12%)	2/1718 (0.12%)

Pneumonia aspiration † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Pneumothorax † [1]		
# participants affected / at risk	**4/1721 (0.23%)**	**2/1718 (0.12%)**
Productive cough † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Pulmonary embolism † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**3/1718 (0.17%)**
Pulmonary oedema † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**0/1718 (0.00%)**
Respiratory acidosis † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Respiratory failure † [1]		
# participants affected / at risk	**4/1721 (0.23%)**	**6/1718 (0.35%)**
Sleep apnoea syndrome † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Sputum increased † [1]		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Skin and subcutaneous tissue disorders		
Angioedema † [1]		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Vascular disorders		
Aortic aneurysm † [1]		
# participants affected / at risk	**2/1721 (0.12%)**	**0/1718 (0.00%)**

Aortic stenosis † 1		
# participants affected / at risk	**2/1721 (0.12%)**	**0/1718 (0.00%)**
Circulatory collapse † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Deep vein thrombosis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Hypertension † 1		
# participants affected / at risk	**2/1721 (0.12%)**	**1/1718 (0.06%)**
Hypertensive crisis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**1/1718 (0.06%)**
Hypertensive emergency † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Hypotension † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Peripheral arterial occlusive disease † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Peripheral artery stenosis † 1		
# participants affected / at risk	**1/1721 (0.06%)**	**0/1718 (0.00%)**
Peripheral ischaemia † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Phlebitis † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**
Varicose vein † 1		
# participants affected / at risk	**0/1721 (0.00%)**	**1/1718 (0.06%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	1.5%

Reporting Groups

	Description
IndIndacaterol	Indacaterol 150 µg o.d., delivered via SDDPI o.d. plus placebo to tiotropium o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®)
Tiotropium	Tiotropium 18 µg o.d. delivered via the manufacturer's proprietary inhalation device (Handihaler®) plus placebo to indacaterol o.d. delivered via SDDPI

Other Adverse Events

	IndIndacaterol	Tiotropium
Total, other (not including serious) adverse events		
# participants affected / at risk	**890/1721 (51.71%)**	**793/1718 (46.16%)**
Gastrointestinal disorders		
Diarrhoea † [1]		
# participants affected / at risk	**26/1721 (1.51%)**	**43/1718 (2.50%)**
General disorders		

Pyrexia † [1]		
# participants affected / at risk	19/1721 (1.10%)	26/1718 (1.51%)
Infections and infestations		
Bronchitis † [1]		
# participants affected / at risk	39/1721 (2.27%)	34/1718 (1.98%)
Influenza † [1]		
# participants affected / at risk	38/1721 (2.21%)	45/1718 (2.62%)
Lower respiratory tract infection † [1]		
# participants affected / at risk	125/1721 (7.26%)	98/1718 (5.70%)
Nasopharyngitis † [1]		
# participants affected / at risk	118/1721 (6.86%)	101/1718 (5.88%)
Upper respiratory tract infection † [1]		
# participants affected / at risk	70/1721 (4.07%)	63/1718 (3.67%)
Upper respiratory tract infection bacterial † [1]		
# participants affected / at risk	139/1721 (8.08%)	127/1718 (7.39%)
Urinary tract infection † [1]		
# participants affected / at risk	31/1721 (1.80%)	26/1718 (1.51%)
Viral upper respiratory tract infection † [1]		
# participants affected / at risk	91/1721 (5.29%)	65/1718 (3.78%)
Musculoskeletal and connective tissue disorders		
Back pain † [1]		
# participants affected / at risk	39/1721 (2.27%)	40/1718 (2.33%)
Nervous system disorders		
Headache † [1]		
# participants affected / at risk	53/1721 (3.08%)	49/1718 (2.85%)

Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease † 1		
# participants affected / at risk	**668/1721 (38.81%)**	**591/1718 (34.40%)**
Cough † 1		
# participants affected / at risk	**107/1721 (6.22%)**	**56/1718 (3.26%)**
Dyspnoea † 1		
# participants affected / at risk	**56/1721 (3.25%)**	**50/1718 (2.91%)**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**63/1721 (3.66%)**	**48/1718 (2.79%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial

results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description:

☑ Principal Investigators are NOT employed by the organization sponsoring the study. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of pooled data (i.e.,data from all sites) in clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Decramer ML, Chapman KR, Dahl R, Frith P, Devouassoux G, Fritscher C, Cameron R, Shoaib M, Lawrence D, Young D, McBryan D; INVIGORATE investigators. Once-daily indacaterol versus tiotropium for patients with severe chronic obstructive pulmonary disease (INVIGORATE): a randomised, blinded, parallel-group study. Lancet Respir Med. 2013 Sep;1(7):524-33. doi: 10.1016/S2213-2600(13)70158-9. Epub 2013 Aug 21.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00845728 History of Changes
Other Study ID Numbers:	**CQAB149B2348** 2008-007944-33
Study First Received:	February 15, 2009
Results First Received:	July 3, 2013
Last Updated:	September 16, 2013
Health Authority:	United States: Food and Drug Administration Austria: Federal Office for Safety in Health Care Slovakia: State Institute for Drug Control Canada: Health Canada Israel: Ministry of Health Spain: Spanish Agency of Medicines Estonia: The State Agency of Medicine Lithuania: State Medicine Control Agency - Ministry of Health Finland: Finnish Medicines Agency Belgium: Federal Agency for Medicinal Products and Health Products United Kingdom: Medicines and Healthcare Products Regulatory Agency France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) India: Drugs Controller General of India Hungary: National Institute of Pharmacy Iceland: Icelandic Medicines Control Agency Colombia: INVIMA Instituto Nacional de Vigilancia de Medicamentos y Alimentos Australia: Department of Health and Ageing Therapeutic Goods Administration Denmark: Danish Medicines Agency Czech Republic: State Institute for Drug Control Turkey: Ministry of Health Latvia: State Agency of Medicines Philippines: Bureau of Food and Drugs Russia: FSI Scientific Center of Expertise of Medical Application Germany: Federal Institute for Drugs and Medical Devices Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Portugal: National Authority of Medicines and Health Products (INFARMED, I.P.) Taiwan: Department of Health Sweden: Medical Products Agency Switzerland: Swissmedic

Romania: National Medicines Agency
Peru: Instituto Nacional de Salud
Costa Rica: Ministry of Health Costa Rica
Italy: The Italian Medicines Agency
South Africa: Medicines Control Council
China: Food and Drug Administration
Venezuela: Ministry of Health and Social Development
Brazil: National Health Surveillance Agency
Thailand: Food and Drug Administration
Mexico: National Institute of Public Health, Health Secretariat
New Zealand: Ministry of Health