tion of chronic obstructive pulmonary disease (AECOPD) and pneumonia occupy significant proportion of acute hospital beds. There is therefore an increasing focus on intermediate care initiatives to facilitate early supported discharge (ESD) and admission avoidance (AA) in such patients. Since 10.11.08, our hospital in partnership with Community Intervention Team (C.I.T.) provided service for administration of intravenous (IV) medications, facilitating ESD/AA.
Aim: To evaluate the AMNCH/C.I.T. IV service, in terms of safety, readmission rates, adverse events, bed-days saved, patient satisfaction and cost-effectiveness.
Results: Up to 31.1.11, of 285 patients referred to this service, 32% had a primary diagnosis of acute respiratory illness. 44 patients were male, 48 female. Mean age was 58.5 years (range 18-95). ESD and AA was facilitated in 67% and 33% respectively. Respiratory diagnoses were: pneumonia (n = 63), AECOPD (n = 7), exacerbation of asthma (n = 4), exacerbation of bronchiectasis (n = 5) and non-pneumonic respiratory infection (n = 13). IV treatment saved a minimum of 486 bed-days. Average length-of-stay in the service was 5.3 days. Readmission rate was 3.2%. No adverse incidents were reported. Patient satisfaction was 100%. We estimate that home treatment of these patients saved €457,300 for AMNCH compared to equivalent treatment in hospital.
Conclusion: We conclude that the service continues to be a safe, effective, inexpensive modality for ESD/AA in patients, with significant bed-days and cost-savings for AMNCH.

4678
Potential economic savings of administration of home intravenous antibiotic therapy to patients with acute respiratory infections in Ireland
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Introduction: Acute respiratory infections (ARI) account for a significant proportion of prolonged hospital stays. Intermediate care initiatives supporting home intravenous antibiotics (HIVA) aim to facilitate early discharge and avoid unnecessary admissions. Numerous studies have demonstrated the efficacy of HIVA for acute infections. International studies have shown increased patient satisfaction, improved quality of life, fewer investigations, less cross-infections, decreased social disruptions and increased cost-effectiveness.
Objective: The purpose of this study was to analyse the potential cost-effectiveness of HIVA in patients with ARI in Ireland.
Methods: Using the Health Service Executive (HSE) Casemix and assuming a 60% uptake of ARI patients satisfying HIVA criteria with a length of stay (LOS) of 1-3 days, cost-estimates relating to cost/bed and LOS were used to calculate cost/bed-day savings if HIVA is introduced.
Results: The approx. annual admission rate for ARI conditions such as pneumonia, COPD, asthma, CF and bronchiectasis is 26,700 patients/yr with an average cost per admission of €70,600. Based on an average LOS of 9.2 days at a cost/bed day of €1,920, the cost/ARI admission is €17,664. This equates to €473m. An LOS of 1-3 days would result in cost-estimates of €51.4-154.2m, a gross difference of €318.8m. Accounting for expenses such as capacity, staff, training, equipment, travel and others, we estimate bed-day savings of €200-220m/yr.
Conclusion: HIVA administration is a safe, cost-effective alternative in suitable patients with ARI, potentially providing significant savings to the health service in Ireland.

4679
A prospective re-audit of admissions and discharge delays occurring in patients admitted to a district general hospital's respiratory ward in the United Kingdom
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Introduction: The National Confidential Enquiry into Patient Outcome and Death recommends that following initial assessment and treatment, patients should be transferred to a ward which is appropriate for their clinical condition.
Objective: To assess delays prior to discharge for patients (respiratory vs non-respiratory) whom are medically fit for discharge, following a reduction in respiratory beds from 62 to 46 as recommended by Sarker et al 2010.
Methods: A prospective 2-week audit was conducted on respiratory wards and in-

A summary table comparing the current re-audit to the previous initial audit

		Chadwick et al	Sarkar et al
Total number of patients		109	141
Number of patients	Primary respiratory diagnosis	70	96
	Primary non-respiratory diagnosis	38	45
Mean age of patients(yrs)	Respiratory group	62	68
	Non-respiratory group	72	67
Number of male vs female patients	Respiratory group	31 vs 78	40 vs 101
	Non-respiratory group	22 vs 87	25 vs 116
Average length of stay for all patients(days)		14	13
Total number of patients with delayed discharge		14	75
Average delay in days	Respiratory group	10	8
	Non-respiratory group	11	15

483. The impact of the organisation of care on costs: the role of the physician in home care

4677
An evaluation of the safety, efficacy and cost-effectiveness for patients with acute respiratory illness, of a community-based intravenous medication service: The first 26 months
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Background: Patients with acute respiratory illnesses such as acute exacerba-

cluded patients admitted under three respiratory consultants. Information collated: date of admission and of discharge, age, primary medical diagnosis and reason for delay.
Results:
Conclusions: A reduction in respiratory beds lead to a reduction in patients with delayed discharge regardless of the underlying medical diagnosis. All delays were still attributable to social reasons. Efficient triage and transfer to appropriate wards on admission will further reduce the number of delayed discharges.

4680
The attitude of physicians for asthma treatment and results in the inhaler market between 2004-2009 in Turkey
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We evaluated the effects Turkey Conversion Programme in Health in 2004 on drug market used for treatment of asthma.
We analyzed the data from IMS the programme following the drug market and the data from the Social Security Institution (SSI) for comparative studies.
In 2004 SSI paid nearly 4.0 billion Euro for drugs which increased to 8,5 billion (110%).Inhaler dust asthma drugs was 88.9 million and increased to 280.6 million (3.16 fold). Drug prescribed was 6.037.172 and increased to 20.848.085 boxes (3.45 fold).In the market of subgroup for inhaler dust asthma drugs distribution was; the rescue drugs 31.5%, combined drugs 17.7%, nebules 10.5%.The rates in 2009 were 20.2%, 29.6% and 18% respectively. Economically distribution was; 48.4% for combined drugs, 6.3% for nebules and 6.3% for rescue drugs.Rates for 2009 were 58.4%, 9.2% and 4.1%.The number of rescue drugs increased from 1.901.938 boxes to 4.220.664 (2.22 folds). The financial increase was 4.62 fold from 5.570.177 to 25.739.326.The number for nebules was 631.184 and increased to 3.762.806 (5.96 fold) the cost for them was 5.570.177 increased to 25.739.326 (4.62 fold).The combined drug subgroup the number of prescriptions were 1.066.486 increased to 6.178.315 (5.79 fold).The cost was 43.006.559 and increased to 163.814.343.
There has been an increase in the costs for inhaler drugs used for asthma treatment.Our analyses showed that this increase mostly caused by increase in the number of prescribed combined drugs. This increase we believe decreased the need for rescue drugs but had no effect on the nebules that has been used

4681
Stepping up the controller medication in asthma patients: Impact of various treatment options on costs
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Introduction: To compare asthma-related costs among adults who step-up their controller medication.
Methods: A population-based study was conducted using the administrative health data of British Columbia, Canada (1997 to 2007). Hospitalization, physician visits, and prescription records were used to identify asthma patients (age 14-65) and calculate direct costs. Four cohorts were constructed as those who: increased the dose of inhaled corticosteroids (ICS+ group), switched to ICS/long-acting beta-agonist (LABA) in a single formulation (ICS/LABA group), added LABA in separate formulations (ICS+LABA group), or added leukotriene receptor antagonist (ICS+LRA group). The outcome was the direct cost of asthma (2008 CAD) in the year after the step-up, adjusted for multiple demographic, resource use, and comorbidty variables from the previous year.
Results: 32,640 patients (average age 42.3; 60.3% female) were included (7,115 ICS+, 19,457 ICS/LABA, 4,086 ICS+LABA, and 1,982 ICS/LRA). The average costs of asthma for the year after the index date for the ICS+ group was $509. Compared to ICS+, all other groups had significantly positive incremental costs: +$358.0 for ICS/LABA, +$504.3 for ICS+LABA, and +$541.6 for ICS/LRA (all P-values$<$0.01). Higher age, higher resource use, and higher cumulative dose of rescue medication in the year prior to the step-up date were predictors of higher costs after the step-up date (all p$<$0.01).
Conclusions: Based on relatively large sample and adjusted for several potential confounders, increasing ICS dose as a step-up approach was associated with the lower costs compared to addition of a second class of controller medication.

4682
The cost and diagnostic efficacy of microbiological evaluation of exudative pleural effusion
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Purpose: To evaluate the cost and diagnostic efficacy of microbiological studies of pleural fluids.
Method: Hospitalized patients with exudative pleural effusion were prospectively evaluated. The fluid samples were examined for Gram stain, acid-fast bacilli smear together with specific bacterial, fungal and mycobacterial cultures.
Results: Bacteriologic and EZN stains of the pleural fluids were negative in 89 cases included whereas fluid cultures were positive in 9 (10,1%) cases [3 (12,5%) of the 24 with tuberculous pleurisy and 6 (28,5%) of the 21 with empyema or other parapneumonic pleural effusion]. The cultures of the malignant, nonspecific and paramalignant fluids were negative. In cases with empyema or other parapneumonic pleural effusion and tuberculous pleurisy, no significant difference was determined between culture-positive and culture-negative cases regarding age, gender, fever or fluid LDH and glucose levels; positive cultures were more frequent in the presence of fluid purulence (55.6% versus 8.3%, p=0.046). In 5 (83.3%) of the 6 culture-positive and in 6 (40%) of the 15 culture-negative cases with empyema or other parapneumonic effusion, change in antibiotic treatment was necessary. The costs of the microbiological studies was 39.4 Euro for each case and 1735 Euro and 1419 Euro for cases with noninfectious and infectious fluids, respectively.
Conclusion: Diagnostic yield of the routine microbiological studies of pleural fluids was determined low. It was concluded that requesting microbiological studies of pleural fluids in cases strongly considered to have infection on clinical basis and/or in cases with purulent fluid would be more beneficial regarding diagnostic yield and cost.

484. Translational models of airway disease

4683
Bitter taste receptor agonists as a novel class of bronchodilators in guinea-pig airways
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Rationale: Deshpande et al. (Nat Med 2010) reported that several bitter taste receptor (TAS2R) agonists evoked relaxation of mice and human airways. We examined the effects of three prototype agonists in segments of guinea pig trachea (GPT).
Methods: GPT was pre-contracted with 0.1 μM carbachol in both absence and presence of 3 μM indomethacin or prostaglandin antagonists. The segments were either exposed to denatonium, chloroquine or saccharin, or kept untreated. Expression of TAS2Rs in guinea pig tracheal epithelium and smooth muscle was measured with real-time PCR.
Results: Denatonium and chloroquine induced concentration-dependent relaxations whereas saccharin had no effect. In consistency with these findings, there was expression of TAS2R4 and TAS2R10 for denatonium, and TAS2R3 and TAS2R10 for chloroquine, but not of TAS2Rs for saccharin in guinea pig airways. Denatonium was 6.1-fold more potent than chloroquine (pEC_{50} 4.7±0.1 and 3.8±0.1, respectively). Indomethacin had no effects on the potency of denatonium and chloroquine. However, the magnitude of the denatonium-induced relaxation (57.5±5.2%; n=8) was enhanced by indomethacin (97.7±2.3%; n=8) and the prostaglandin E_2 receptor (EP_1) antagonist ONO-8310 (99.3±0.7; n=5). Chloroquine induced almost complete relaxation (98.2±1.1%; n=6) that was unaffected by indomethacin (99.9±0.04%; n=7).
Conclusion: Denatonium and chloroquine induced relaxation of GPT and their respective TAS2Rs were expressed. There was an interaction between denatonium and PGE_2 acting on EP_1 receptors. The findings support the concept that airway TAS2Rs represent a novel target for anti-asthmatic therapy.

4684
Prostacyclin modifies VEGF synthesis in fibroblasts from healthy and COPD patients
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Background: Involvement of vascular remodelling in the lung is a characteristic sign in chronic obstructive lung disease (COPD). The vascular mediator prostacyclin may regulate fibroblast activity. The objective was to study the effect of prostacyclin on synthesis of vascular endothelial growth factor (VEGF) and interactions with transforming growth factor (TGF) B_1 in distal lung fibroblasts from patients with COPD and control subjects.
Method: Primary human lung fibroblast cultures were established from peripheral airway biopsy samples from healthy individuals (controls, n=5) and after lung resection from patients with COPD (GOLD IV) (n=7). The lung fibroblasts were cultured in 0.4% medium and stimulated with the cyclooxygenase inhibitor indomethacin 3μM in combination with the prostacyclin analogue iloprost 1μM and TGF-B 10ng/ml for 24h. VEGF production was measured in the cell culture supernatant by ELISA.

Results: Iloprost enhanced VEGF synthesis in both fibroblasts from control subjects (774±171 vs 438±55 pg/ml, $p<0.05$) and patients with COPD (350±34 vs 512±81 pg/ml, $p<0.05$). TGF-B increased the production of VEGF 5-fold in fibroblasts from control subjects ($p<0.05$) and 6.1-fold from patients with COPD ($p<0.01$). However, iloprost showed no effect on VEGF synthesis after TGF-B stimulation, whereas indomethacin reduced VEGF production in fibroblasts from patients with COPD ($p<0.05$) but not in control subjects.
Conclusions: Iloprost enhanced VEGF synthesis in fibroblasts from both healthy and patients with COPD. Though, iloprost had no effect on VEGF after TGF-B_1 stimulation. This data implicate that also other prostanoids are involved in the regulation of VEGF in fibroblasts from COPD patients.

4685
Capsazepine inhibits NF-κB subunits in dsRNA-exposed human bronchial epithelial cells from asthmatic and COPD donors
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Background: Novel drugs are needed to treat viral-induced exacerbations of asthma and COPD. We have shown that capsazepine (CPZ) inhibits viral-induced cytokine production (including thymic stromal lymphopoietin, TSLP) in human asthmatic bronchial epithelial cells (HBEC) more effectively than steroids.
Objective: Investigate NF-κB mechanisms potentially involved in actions of CPZ in HBECs from patients with asthma and COPD.
Methods: Primary HBEC were obtained by fibre optic bronchoscopy from individuals with asthma (n=6) and COPD (n=3), then grown in 12-well plates and stimulated with viral surrogate dsRNA (10 μg/ml) to induce pro-inflammatory cytokine (TSLP, TNF-α, IL-8, IFN-β) mRNA expression (RT-qPCR) and production (ELISA). CPZ (3-30 μM) was added 1 h prior to dsRNA. NF-κB-signaling was studied (western blot) using specific antibodies for NF-κB subunits p65, p105 and IκB-α. De novo gene synthesis of IκB-α was studied by RT-qPCR.
Results: dsRNA induced marked expression and release of TSLP, TNF-α, IL-8, and IFN-β ($p<0.001$). These effects were dose-dependently reduced ($p<0.05$-$p<0.001$) by CPZ that also tended to inhibit TSLP more than IFN-β ($p=0.09$). dsRNA induced degradation and de novo gene synthesis of IκB-α and increased the release of p65 and p105 ($p<0.01$). CPZ prevented the degradation of IκB-α and inhibited p65 and p105.
Conclusion: CPZ effectively reduced dsRNA-induced cytokine overproduction in HBECs from asthmatic and COPD donors. CPZ inhibited dsRNA-induced IκB-α degradation preventing dissociation and translocation of p65 and p105 to the nuclear NF-κB promoter. CPZ may stabilize IκB-α thus inhibiting NF-κB-dependent cytokine production.

4686
Bradykinin-induced contractions in guinea pig trachea after incubation and culture
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Background: Inflammatory conditions can alter responsiveness to the endogenous mediator bradykinin (BK) in mouse and human airway smooth muscle. Guinea-pig and human airways generally display similar smooth muscle responsiveness. The aim of this study was to develop an *in vitro*-model in guinea pig trachea (GPT) to study the regulation of BK responses by culture procedures.
Methods: The contractile response to BK was determined in organ tissue baths. Either fresh, organ bath incubated (6-12 hours) or in DMEM/ F12 media cultured (4 days) GPT segments were used for these measurements. The contractile responses to BK were determined in the presence of 3μM indomethacin and 10μM captopril. Contractions were presented as a percentage of the maximal contraction of the GPT.
Results: In fresh GPT, BK induced only weak contractions (E_{max}: 8±2%). This response was not changed after 6 hours incubation, however after 12 hours incubation a strong enhancement of the BK induced contraction was observed (E_{max}: 53±2%, pEC_{50} 7.4±0.2). This up-regulated response was partly regulated by prostanoids, since both E_{max} (28±2%) and pEC_{50} (6.3±0.1) were decreased in segments incubated for 12 hours with indomethacin. In contrast to the 12-hour incubation in the tissue bath, the contractile response to BK after 4 days organ culture was only slightly enhanced (E_{max}: 21±3%).
Conclusion: This study shows that contractions in GPT to BK are inducible over time. The different effects of incubations in the tissue bath and the organ culture may be used to study different aspects of regulation of BK responsiveness in airway inflammation.

4687
Protective effect of a protein epitope mimetic (PEM) CCR10 antagonist, POL7085, in an allergic model of asthma
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Potential involvement of the CCR10/CCL28 axis was recently reported in a murine model of allergic asthma [1]. Blockade of the CCR10 receptor might therefore represent a novel alternative to the current treatment of asthma. We have evaluated the effect of the PEM CCR10 antagonist, POL7085, in an allergic model of asthma in mice. Nine week-old male Balb/c mice were sensitized to ovalbumin (OVA) administered intraperitoneally in the presence of alum (D0 and D7), and challenged to OVA administered intranasally (D18 to D21). POL7085 was administered once daily 1 hour before each OVA challenge at 9 and 18mmol/kg intra-nasally (I.N.) *vs* dexamethasone I.N. (DEX; 2.3mmol/kg) *vs* vehicle.
In vehicle treated animals, OVA induced airway hyperresponsiveness (AHR) as measured by whole body plethysmography, and hypereosinophilia in the bronchoalveolar lavage (BAL) fluid. POL7085 dose-dependently and significantly decreased AHR by 34±16% and eosinophil numbers in BAL by 66±6%. In addition, the higher dose of POL7085 also inhibited IL-5 secretion in BAL (42±13%), IgE and IgG1 synthesis in serum (47±31% and 61±15%, respectively), and lung collagen synthesis (43±11%), although not significantly. POL7085 as compared to DEX also modified body (6.5±1.7% *vs* 4.5±1.5% for DEX) and spleen weight (24±3% *vs* 44±3% for DEX).
In conclusion, the PEM CCR10 antagonist, POL7085, significantly and dose-dependently decreased asthma symptoms after once daily local administration, in particular AHR and eosinophilia. Blocking the CCR10 chemokine receptor therefore appears as a promising novel approach for treating asthma.
Reference:
[1] English et al, Immunol Lett; 2006;103:92-100.

4688
Characterisation of TNF-alpha lectin-like domain derived peptides associated with improved alveolar fluid clearance in pulmonary oedema
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The beneficial effect of the lectin-like domain of TNF-alpha, including the TIP peptide which mimics this domain, on activation of oedema resorption, improved alveolar clearance and protection of lung function after transplantation, is well documented from several independent *in vitro and in vivo* studies using animal models. The effect is mediated by activation of sodium uptake through the amiloride-sensitive epithelial sodium ion channel (ENaC), which plays a major role in alveolar fluid clearance in normal and diseased lungs. Several peptides mimicking the lectin-like domain of human TNF-alpha, and differing from the human TIP peptide by mutation or substitution of amino acid residues with non-natural derivatives, were synthesised and tested for their ability to enhance sodium current through ENaC in A549 cells with the patch clamp technique.
For all ENaC-activating TIP peptides a maximum effect was observed at 120 nM. Compared to TNF-alpha (EC_{50} 8.2 nM) and the original human TIP peptide (EC_{50} 54.3 nM), several of the newly-designed peptides were more effective at enhancing amiloride-sensitive current than the latter: the most active peptide had an EC_{50} of 19.9 nM. Our data suggest that TIP peptides with charge distribution and interatomic distances most closely resembling the 3D structure of the native lectin-like domain of TNF-alpha, are those with greater ability to enhance activation of sodium current through ENaC. No standard therapy exists for pulmonary oedema, thus these TIP peptides represent promising therapeutic agents for activating sodium uptake from the alveolar fluid through ENaC and improving clinical outcome in this condition.

4689
Consequences of chronic pulmonary TLR9 activation in the lung and beyond
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Background: Toll like receptor 9 (TLR9) agonist CpG-ODN is being explored as an anti-allergic drug for asthma. However TLR9 could play a role in COPD. Cigarette smoke induced IL-8 production is partly TLR9 mediated.
Aim: To investigate the (extra)-pulmonary effects of CpG-ODN. We hypothesized that pulmonary TLR9 activation induces neutrophil influx which could lead to adverse effects.
Methods: A single dose of 0.01, 0.05 or 0.25nMol/gBW GpG-ODN was targeted to balb/c mice lungs by aspiration (acute). Next 0.01nMol/gBW GpG-ODN was administered repeatedly for 5 days (subchronic) or 5 weeks (chronic). 24 hours after last exposures, measurements were done: lung function; hypertension and

heart hypertrophy; lung weight; blood and bronchoalveolar lavage (BAL) analysis; morphology of unlavaged lungs.
Results: Total BAL cells were increased in all CpG-ODN mice ($p<0.05$). PMNs were increased in blood (30%) and BAL (39%) acute which persistent upon prolonged exposure duration. Blood lymphocytes were subchronically 19% decreased which was reflected in an abundant pulmonary (sub)- chronic lymphocyte influx. Chronic exposure leads to 21% decreased peak expiratory flow (ml/sec) and 71% increased airway resistance (cm H2O/ml/sec). Right ventricle heart hypertrophy was observed upon chronic exposure; ratio right ventricle weight/total heart weight CpG-ODN=0.23±0.007; control=0.19±0.008. Wet lung weight was 15.2% increased subchronically and 70.8% chronically.
Conclusion: An interplay between neutrophils and lymphocytes could possibly play a role in TLR9 induced adverse pulmonary and cardiovascular effects. Caution is needed when CpG-ODNs are chronically administered for therapeutical purposes.
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4690

Efficacy of the TRPV1 antagonist SB-705498 in an MRI guinea pig model of rhinitis

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Rationale: Antagonism of nasal TRPV1 receptors is a potential target for inhibition of symptoms associated with rhinitis. Here, we explore the pharmacology of SB-705498 on the contralateral nasal secretory response to ipsilateral nasal capsaicin challenge in the guinea pig.
Methods: Experiments were conducted on intranasally sensitised guinea pigs. Absolute nasal fluid volumes were measured using MRI techniques that provide images of the total nasal cavity of the guinea pig. Animals were pre-treated with SB-705498 or vehicle (-1, -6 and -24h) and MRI scanned to produce first a baseline measurement and then a further measurement at 10 minutes post capsaicin challenge (0.3mM; 50ul).
Results: 1 hour pre-treatment with SB-705498 resulted in approximately 50% inhibition of the secretory response at 10mg/kg (oral; $p<0.05$), 1mg/kg (intranasal suspension; $p<0.005$) and 0.1mg/kg (intranasal particle reduced suspension; $p<0.0005$). At 12 hour pre-treatment, approximately 60% inhibition ($p < 0.0001$) was observed with SB-705498 at 1mg/kg (intranasal particle reduced suspension); at 24h this had reduced to ~50% inhibition ($p<0.01$).
Conclusion: These studies demonstrate that SB-705498 inhibits capsaicin-induced intranasal parasympathetic responses in guinea pig. Topical application of SB-705498 was associated with a approximately 10-fold reduction in total dose compared with oral administration. In addition, particle reduction of SB-705498 was associated with a further improvement in intranasal potency.