CORESTA

Cooperation Center
for
Scientific Research Relative to Tobacco

A meeting with FDA's Center for Tobacco Products – Office of Science

21 January 2011

Agenda

- **Introduction**
  - Mike Ogden – President of the Board
- **Overview of CORESTA organisation**
  - Pierre-Marie Guitton – Secretary General
- **Overview of CORESTA scientific program**
  - Jean-Louis Verrier – President of the Scientific Commission
  - Derek Mariner – Vice-President of the Scientific Commission
- **CORESTA Special Analytes Sub-Group**
  - Steve Purkis – President of the Smoke Science Study Group
    Coordinator of the Special Analytes Sub-Group
- **Discussion**

CORESTA Organisation

Introduction to CORESTA

- **CORESTA is the Cooperation Centre for Scientific Research Relative to Tobacco**
- **It is an Association:**
  - ✓ **Founded in 1956**
  - ✓ **Headquartered in Paris**
  - ✓ **Governed under French law**
- **The name "CORESTA" derives from the historic full title of the Association:**

Centre de
Coopération pour les Recherches Scientifiques Relatives au Tabac

The Purpose of CORESTA

Encourage international cooperation

to actively work

on tobacco-related areas of research

The Structure

- **CORESTA members are organisations, not persons**
- **Each member organisation mandates one official delegate to elect:**
  - ✓ **a Board of 10 member organisations (+ 2 to 4 co-opted) with the responsibility of governing the Association**
  - ✓ **a Scientific Commission of 20 scientists (5 x 4 Study Groups) with the responsibility of initiating, leading and monitoring the scientific work within CORESTA, in liaison and with the approval of the Board**

Working Groups

Organised within Study Groups,
they each focus on one particular issue with clear objectives

Sub-Groups (SG)

deal with a permanent or long-term issue

Task Forces (TF)

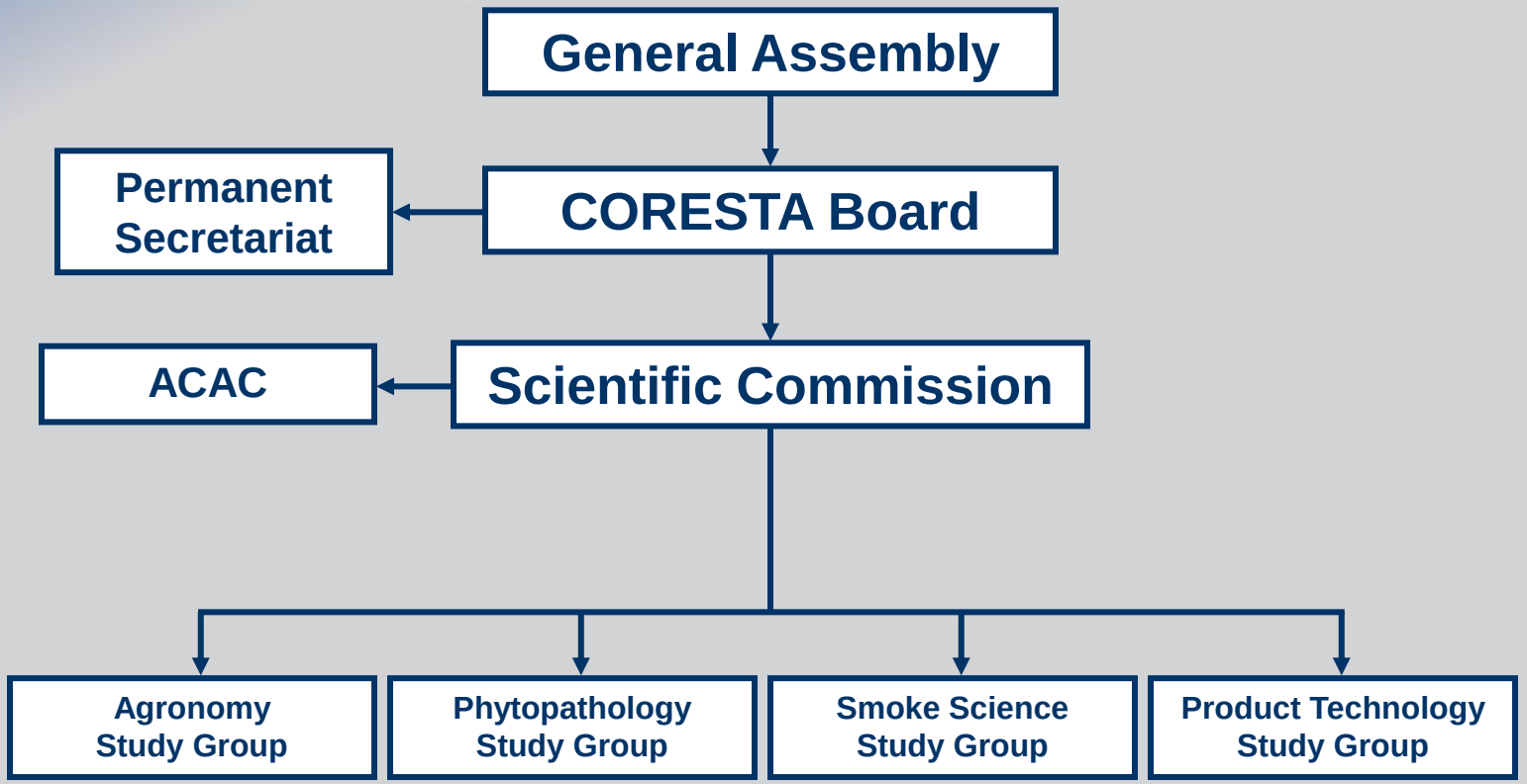
deal with a specific topic well defined in a mandate
within a limited time-frame

In addition,

an Agrochemicals Advisory Committee (ACAC)
is under the direct supervision of the Scientific Commission

ACAC members are co-opted

The Structure



The Board

President: Dr. Michael Ogden

R.J. Reynolds Tobacco Co. (USA)

Vice-President: Dr. Martin Ward

British American Tobacco – Group R&D (UK)

Secretary General: Pierre-Marie Guitton

CORESTA (France)

Member Organisations

- ✓ Alliance One International Inc. (USA)
- ✓ Borgwaldt KC (Germany)
- ✓ British American Tobacco (UK)
- ✓ China National Tobacco Corp. (China)
- ✓ Imperial Tobacco Ltd. (UK)
- ✓ Japan Tobacco Inc. (Japan)
- ✓ KT&G Corp. (South Korea)
- ✓ Papierfabrik Wattens GmbH & Co. KG (Austria)
- ✓ R.J. Reynolds Tobacco Co. (USA)
- ✓ SWM International Inc. (France)
- ✓ Sodim S.A.S. (France)
- ✓ Swedish Match North Europe Division (Sweden)
- ✓ Tann-Papier GmbH (Austria)
- ✓ Universal Leaf Tobacco Co. (USA)

The Scientific Commission

President: Dr. Jean-Louis Verrier

Imperial Tobacco Group - Institut du Tabac de Bergerac (France)

Vice-President: Dr. Derek Mariner

British American Tobacco – Group R&D (UK)

- **Agronomy Study Group**
  - ✓ Dr. Marco Prat (JT International Germany GmbH, Germany)
  - ✓ Lea Scott (Universal Leaf Tobacco Co., USA)
  - ✓ Dr. Davis Martin (F.W. Rickard Seeds Inc., USA)
  - ✓ Mario Bender (Premium Tabacos do Brasil, Brazil)
- **Phytopathology Study Group**
  - ✓ Anne Jack (University of Kentucky, USA)
  - ✓ Dr. Dongmei Xu (Altria Client Services, USA)
  - ✓ Prof. Teresa Doroszewska (Institute Soil Sci. & Plant Cult., Poland)
  - ✓ Dr. Cheong-Ho Lee (KT&G Central Research Institute, South Korea)

The Scientific Commission

- **Smoke Science Study Group**
  - ✓ Steve Purkis (Imperial Tobacco Group, UK)
  - ✓ Dr. Charles Garner (R.J. Reynolds Tobacco Company, USA)
  - ✓ Dr. Derek Mariner (British American Tobacco, UK)
  - ✓ Kei Yoshino (Japan Tobacco Inc., Japan)
  - ✓ Dr. Hyo-Keun Kim (KT&G Central Research Institute, South Korea)

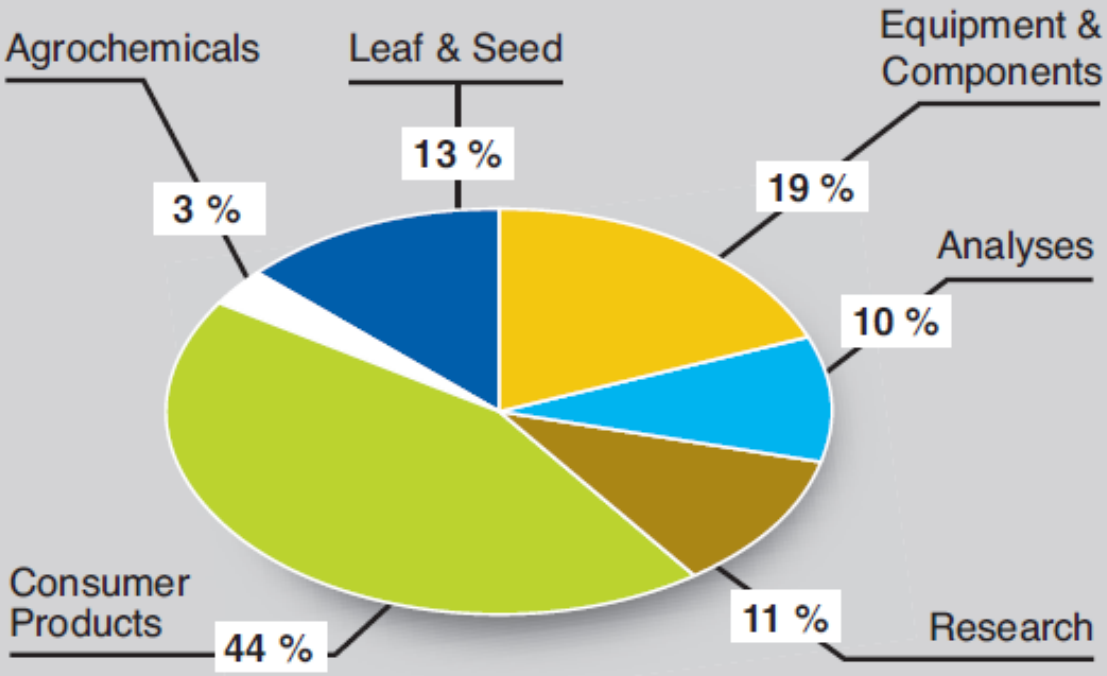
- **Product Technology Study Group**
  - ✓ Nick Boham (British American Tobacco, UK)
  - ✓ Dr. Marc Scharfe (Heintz Van Landewyck, Luxemburg)
  - ✓ Linda Crumpler (Cerulean, USA)
  - ✓ Chuanfang Yu (Zhengzhou Tobacco Research Inst., China)
  - ✓ Dr. Christophe Le Moigne (SWM International Inc., France)

General Secretariat

- **The Head Office in Paris hosts a General Secretariat**
- **The General Secretariat is in charge of:**
  - ✓ **Keeping general documentation**
    - Reports and Methods issued by Study Groups
    - Papers and Posters from Meetings & Congresses
    - Internal and external data bases
  - ✓ **Preparing the annual meetings**
  - ✓ **Providing support to CORESTA members**
    - Circulation of information
    - Official and legal documents
    - Membership
    - General co-ordination

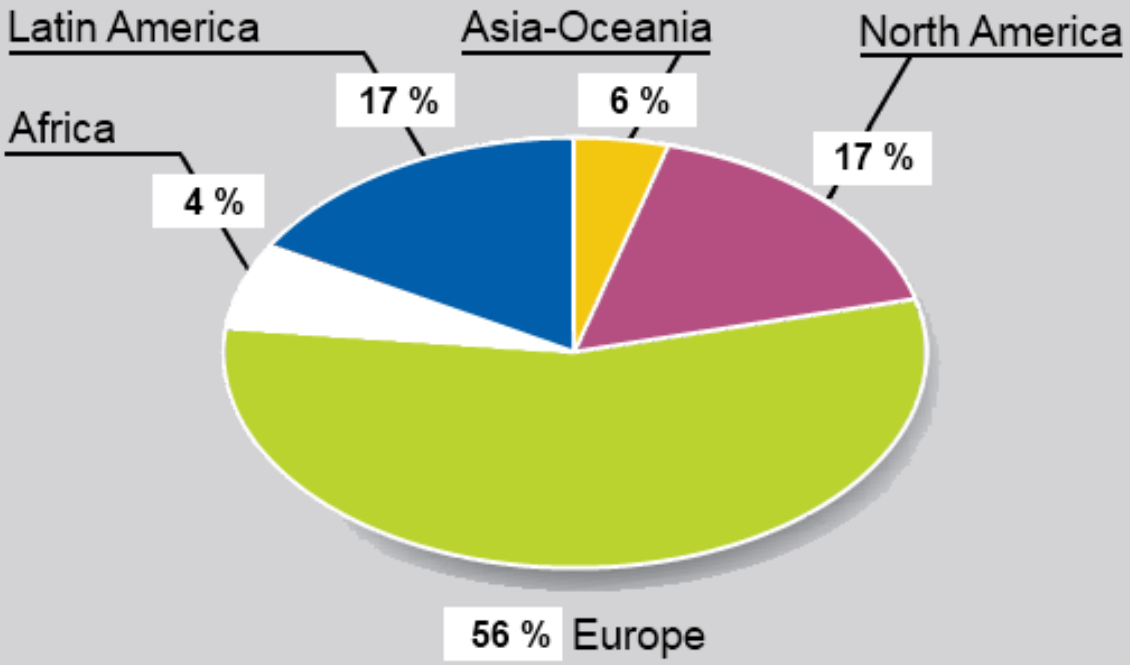
Membership
(by Industry Sector)

- **An annual membership is renewed in April**
  - ✓ **178 paid membership fees in the current year**



Membership
(by Geographic Region)

- **An annual membership is renewed in April**
  - ✓ **178 paid membership fees in the current year**



Meetings

- **Participation in Sub-Group, Task Force or Committee activities remains at member-organisation discretion and expense**
  - ✓ **Some 500 delegates participate in one (or more) group**
- **Congresses and Group Meetings are hosted and organised by volunteering member organisations**
  - ✓ **Congresses in even years**
    - All Study Groups
    - General Assembly and Elections
      - Next meeting: 23-28 September 2012 – Sapporo, Japan
  - ✓ **Joint Meetings in odd years**
    - Agronomy & Phytopathology
      - Next meeting: 23-26 October 2011 – Santiago, Chile (to be confirmed)
    - Smoke Science & Product Technology
      - Next meeting: 9-13 October 2011 – Graz, Austria

Will be held in Santiago, 6-10 November

CORESTA Scientific Program

Agro Chemical Advisory Committee (ACAC)

- **Special committee responding directly to the Scientific Commission**
- **Members appointed by Scientific Commission**
- **Objectives of ACAC:**
  - ✓ **Gathering of existing scientific data and regulatory information about agro-chemicals**
  - ✓ **Investigating new agro-techniques**
  - ✓ **Interpreting agrochemical issues within context of industry requirements**
  - ✓ **Informing CORESTA members of emerging issues**

2 x 2 Study Groups

- **Agronomy & Phytopathology**
  - ✓ Agronomy
  - ✓ Pests & plant diseases
  - ✓ Curing
  - ✓ Agrochemical issues

- **Smoke Science & Product Technology**
  - ✓ Technical specifications
  - ✓ Smoke analysis
  - ✓ Analytical standards
  - ✓ Consumer behaviour and toxicology

« Agro-Phyto »

❖ Agronomy

- ✓ SG TSNA in Air-Cured and Fire-Cured Tobacco
- ✓ TF Curing Technology

❖ Phytopathology

- ✓ SG Pest & Sanitation Management in Stored Tobacco
- ✓ SG Collaborative Study on Blue Mould
- ✓ SG Collaborative Study on Nematodes
- ✓ SG GM Tobacco - Proficiency Testing
- ✓ TF Integrated Pest Management (IPM)
- ✓ SG Collaborative Study on Virus Diseases

Achievements

❖ Agronomy & Phytopathology

- ✓ Defined Good Agricultural Practices (GAP) for tobacco and set Guidance Residue Levels for relevant agro-chemicals
- ✓ Promoted industry-wide adoption of GAP
- ✓ Promoted reductions in the risk of crop loss and the use of plant protection agents
- ✓ Edited Guides for the control of insects
- ✓ Organizes a yearly Infestation Control Conference
- ✓ Collects and shares worldwide information on Blue Mould

« Smoke-Techno »

❖ Smoke Science

- ✓ SG Smoking Behaviour
- ✓ SG Special Analytes
- ✓ TF *In Vitro* Toxicity
- ✓ SG Biomarkers

❖ Product Technology

- ✓ SG Agrochemicals Analysis
- ✓ SG Routine Analytical Chemistry
- ✓ SG Physical Test Methods
- ✓ SG Cigar Smoking Methods
- ✓ SG Smokeless Tobacco

Achievements

❖ Smoke Science & Product Technology

- ✓ **Developed 70 Recommended Methods for tobacco, product and smoke analysis (chemical and physical)***
  - 37 ISO standards based on CORESTA Recommended Methods (CRMs)
  - Protocols for *in vitro* toxicity testing of mainstream smoke
  - Regular collaborative studies/proficiency trials to support member labs' accreditation (agrochems, TNCO, physical, *in vitro*)
- ✓ **Developed Reference Materials**
  - CM6 for smoking machine set-up / 4 smokeless tobacco products
- ✓ **Active Sub-Groups for Cigars, Smokeless Tobacco, Smoking Behaviour, Special Analytes, Biomarkers**

***57 CRMs currently active, due to obsolescence/replacement of older ones**

Correlation of CORESTA & ISO Methods (1)

REF.	TITLE	DATE	Bulletin/CD	ISO correlation
N° 1	Determination of Dithiocarbamates in Tobacco	Nov. 1978	1978-2	ISO 6466:1983
N° 2	Determination of Organochlorine Pesticide Residues on Tobacco	May 1997	1997-1	ISO 4389:2000
N° 4	Determination of Maleic Hydrazide Residues in Tobacco	Sep. 1976	1976-2	ISO 4876:1980
N° 5	Determination of Carbon Monoxide in the Mainstream Smoke of Cigarettes by Non-Dispersive Infrared Analysis	Sep. 1993	1993-4	ISO 8454:2007
N° 6	Measurement of Ventilation : Definitions and Measurement Principles	Mar. 2000	2000-1	ISO 9512:2002
N° 7	Determination of Nicotine in the Mainstream Smoke of Cigarettes by Gas Chromatographic Analysis	Aug. 1991	1991-3	ISO 10315:2000
N° 8	Determination of Water in the Mainstream Smoke of Cigarettes by Gas Chromatographic Analysis	Aug. 1991	1991-3	ISO 10362-1:1999
N° 9	Determination of Nicotine in Cigarette Filters by Gas Chromatographic Analysis ***(new edition)***	Apr. 2009	CD 28	ISO 4388:1991
N° 12	Determination of Alkaloids in Cigarette Smoke Condensate	Sep. 1968	1969-2	ISO 3400:1997
N° 13	Determination of Alkaloid Retention by Cigarette Filters	Sep. 1968	1969-2	ISO 3401:1991
N° 15	Cigarettes - Determination of Water in Smoke Condensates - Karl Fischer Method	Mar. 1990	1990-2	ISO 10362-2:1994
N° 16	Lamina Strip Particle Size Determination	Jan. 1991	1991-1	ISO 12194:1995
N° 17	Stem Content of Lamina Strips	Jan. 1991	1991-1	ISO 12195:1995
N° 20	Determination of Alkaloids in Manufactured Tobacco	Sep. 1968	1969-2	ISO 2881:1992
N° 21	Atmosphere for Conditioning and Testing Tobacco and Tobacco Products	Aug. 1991	1991-3	ISO 3402:1999
N° 22	Routine Analytical Cigarette-Smoking Machine: Specifications, Definitions and Standard Conditions	Aug. 1991	1991-3	ISO 3308:2000
N° 23	Determination of Total and Nicotine-Free Dry Particulate Matter using a Routine Analytical Cigarette-Smoking Machine Determination of Total Particulate Matter and Preparation for Water and Nicotine Measurements	Aug. 1991	1991-3	ISO 4387:2000
N° 24	Cigarettes – Sampling	Aug. 1991	1991-3	ISO 8243:2006
N° 25	Ambient Air-Flow around Cigarettes in Routine Analytical Smoking Machines : Control and Monitoring	Aug. 1991	1991-3	
N° 30	Determination of Residues of the Suckercide Flumetralin (Prime Plus, CGA-41065) on Tobacco	Jun. 1991	1991-2	
N° 31	Determination of Residues of the Suckercide Pendimethalin (Accotab, Stomp) on Tobacco	Jun. 1991	1991-2	

WARNING: This table was last updated in September 2010. It is made available for the convenience of tobacco researchers and is for information purposes only. The precise correlation or equivalence between CORESTA Recommended Methods (CRM) and ISO Standards has the potential to vary greatly at any point in time because the CRMs and ISO Standards are revised and updated independently.

Correlation of CORESTA & ISO Methods (2)

REF.	TITLE	DATE	Bulletin/CD	ISO correlation
N° 32	Determination of Residues of the Suckercide Off-Shoot-T (N-Alkanol Mixture) on Tobacco	Jun. 1991	1991-2	
N° 33	Determination of Acetate in Cigarette Paper	Jan. 1993	1992-3/4	ISO/PRF 20370
N° 34	Determination of Citrate in Cigarette Paper	Jan. 1993	1992-3/4	ISO/PRF 20369
N° 35	Determination of Total Alkaloids (as Nicotine) in Tobacco by Continuous Flow Analysis	Aug. 2010	CD 31	ISO 15152:2003
N° 36	Determination of Nitrate in Tobacco by Continuous Flow Analysis	Aug. 2010	CD 31	ISO 15517:2003
N° 37	Determination of Reducing Substances in Tobacco by Continuous Flow Analysis	Aug. 2010	CD 31	ISO 15153:2003
N° 38	Determination of Reducing Carbohydrates in Tobacco by Continuous Flow Analysis	Aug. 2010	CD 31	ISO 15154:2003
N° 39	Determination of the Purity of Nicotine and Nicotine Salts by Gravimetric Analysis - Tungstosilicic Acid Method	Nov. 1994	1994-3/4	ISO 13276:1997
N° 40	Determination of Air Permeability of Materials used as Cigarette Papers, Filter Plug Wrap and Filter Joining Paper including Materials having an Oriented Permeable Zone	Oct. 1994	1994-3/4	ISO 2965:2009
N° 41	Determination of the Draw Resistance of Cigarettes and Filter Rods (***new edition***)	Jun. 2007	CD 24	ISO 6565:2002
N° 42	Atmosphere for Conditioning and Testing Fine-Cut Tobacco and Fine-Cut Smoking Articles	Jun. 1997	1997-1	ISO 15592-2:2001
N° 43	Fine-Cut Tobacco - Sampling	Jun. 1997	1997-1	ISO 15592-1:2001
N° 45	Determination of Phosphate in Cigarette Paper	Jan. 1998	1997-4	
N° 46	Atmosphere for Conditioning and Testing Cigars of all Sizes and Shapes	May 1998	1998-1	
N° 47	Cigars – Sampling	Jan. 2000	2000-1	
N° 50	Environmental Tobacco Smoke - Determination of Nicotine and 3-Ethenylpyridine in the Vapour Phase	Jan. 2002	CD 13	ISO 18145:2003
N° 51	Environmental Tobacco Smoke - Estimation of its Contribution to Respirable Suspended Particles - Determination of Particulate Matter by Ultraviolet Absorbance and by Fluorescence	Jan. 2002	CD 13	ISO 15593:2001
N° 52	Environmental Tobacco Smoke - Estimation of its Contribution to Respirable Suspended Particles - Method based on Solanesol Determination	Jan. 2002	CD 13	ISO 18144:2003
N° 53	Determination of Paper Wrapper Burn Speed	May 2002	CD 14	

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Correlation of CORESTA & ISO Methods (3)

REF.	TITLE	DATE	Bulletin/CD	ISO correlation
N° 54	Determination of Nicotine and Nicotine-Free Dry Particulate Matter in Sidestream Smoke using a Fishtail Chimney and a Routine Analytical/Linear Smoking Machine	Jun. 2002	CD 15	ISO 20773:2007
N° 55	Determination of Carbon Monoxide in the Vapour Phase of Cigarette Sidestream Smoke using a Fishtail Chimney and a Routine Analytical/Linear Smoking Machine	Jun. 2002	CD 15	ISO 20774:2007
N° 56	Determination of Water in Tobacco and Tobacco Products by Karl Fischer Method	Dec. 2002	CD 16	ISO 6488:2004
N° 57	Determination of Water in Tobacco and Tobacco Products by Gas Chromatographic Analysis	Dec. 2002	CD 16	ISO 16632:2003
N° 58	Determination of Benzo[a]Pyrene in Cigarette Mainstream Smoke – Gas Chromatography-Mass Spectrometry Method	Feb. 2004	CD 18	ISO 22634:2008
N° 59	Determination of Triacetin in Filter Rods by Gas Chromatographic Analysis	Jun. 2004	CD 20	
N° 60	Determination of 1,2-Propylene Glycol and Glycerol in Tobacco and Tobacco Products by Gas Chromatography	Feb. 2005	CD 20	
N° 61	Determination of 1,2-Propylene Glycol, Glycerol and Sorbitol in Tobacco and Tobacco Products by High Performance Liquid Chromatography (HPLC)	Feb. 2005	CD 20	
N° 62	Determination of Nicotine in Tobacco and Tobacco Products by Gas Chromatographic Analysis	Feb. 2005	CD 20	
N° 63	Determination of Tobacco Specific Nitrosamines in Cigarette Mainstream Smoke - GC-TEA Method	Jun. 2005	CD 20	
N° 64	Routine Analytical Cigar-Smoking Machine - Specifications, Definitions and Standard Conditions	Nov. 2005	CD 21	
N° 65	Determination of Total and Nicotine-Free Dry Particulate Matter using a Routine Analytical Cigar-Smoking Machine – Determination of Total Particulate Matter and Preparation for Water and Nicotine Measurements ***(new edition)***	Jun. 2010	CD 31	
N° 66	Determination of Nicotine in the Mainstream Smoke of Cigars by Gas Chromatographic Analysis	Nov. 2005	CD 21	
N° 67	Determination of Water in the Mainstream Smoke of Cigars by Gas Chromatographic Analysis	Nov. 2005	CD 21	
N° 68	Determination of Carbon Monoxide in the Mainstream Smoke of Cigars by Non-Dispersive Infrared Analysis	Jan. 2010	CD 30	
N° 69	Determination of pH in Smokeless Tobacco Products	Jun. 2010	CD 31	
N° 70	Determination of selected volatile organic compounds in the Mainstream Smoke of Cigarettes – Gas Chromatography Mass Spectrometry Method	Jun. 2010	CD 31	

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CORESTA Special Analytes Sub-Group

Historical Background

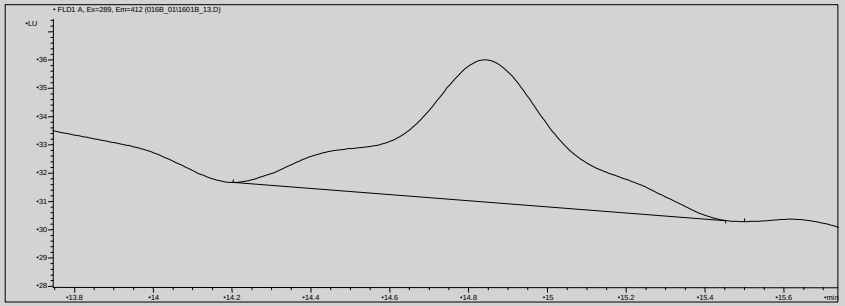
- **Methodologies described for isolating and estimating the yields of smoke components**
  - ✓ Hoffmann et al. papers on newly identified toxicants (1960s ->)
  - ✓ UK methods in 1970s/1980s by industry providing measurements in support of New Smoking Materials ….. subsequent LGC papers giving their methods and measurements
  - ✓ Many reported methodologies by industry and research bodies (e.g., RJR)
- **Methodologies adopted as Health Canada Official Methods in 1999**
  - ✓ Taken from the literature by Labstat
  - ✓ No external discussions on weaknesses or optimisation of methods
  - ✓ No collaborative studies to determine inter-laboratory variability
  - ✓ Protocols not previously tested under CI smoking regime
- **High variability when comparing data from different laboratories using their preferred methodologies**
  - ✓ Methods may be precise (when comparing replicates) but precisely wrong (when compared to other labs)!
- **Benchmarking approach**
  - ✓ Range of products analysed by a particular method used in a particular laboratory at one point in time
  - ✓ Approach excludes potential inter-laboratory variability (e.g., MA, Canada, UK, Australia)
  - ✓ If not all analyses done at one point in time then misinterpretation still possible (Australia)

Standardised Methods

- **Robust TNCO methods standardised with known measurement tolerances**
  - ✓ **Allow comparisons of product yields tested after manufacture with yields obtained by regulatory verification laboratories**
- **Methodologies for smoke components other than TNCO**
  - ✓ **Need for standardisation**
    - Methods not standardised prior to introduction of Health Canada regulations
  - ✓ **Data from methodologies may not be meaningful**
  - ✓ **Tolerances around measurements or ceilings not established**
- **CORESTA decided to set up a Task Force in 1999 to produce Recommended Methods**
  - ✓ **15 laboratories initially interested in participating in work if their equipment capability allowed (i.e., method dependent)**
  - ✓ **Priority compounds identified as benzo[a]pyrene and 4 TSNAs (with work based on Health Canada methods)**
  - ✓ **Methods intended to be submitted to ISO when sufficiently robust**
  - ✓ **Variability expected to be higher than TNCO values because component yields are measured in µgs or ngs rather than mgs**

Benzo[a]pyrene

- Several collaborative studies between 1999 and 2003
- Two methodologies studied under ISO smoking
  - ✓ Firstly HPLC with fluorescence detection and secondly GC-MS
  - ✓ Smoke clean-up required in both cases to obtain good separation
  - ✓ HPLC studies gave high variability between laboratories due to poor separation from other components
  - ✓ GC-MS method gave lower variability but still high!!
  - ✓ Yield expected to be mean ± R
  - ✓ R% given for comparisons across analytes
  - ✓ Collaborative involved 13 laboratories
  - ✓ CRM 58 published (2004)
  - ✓ ISO 22634 published (2007)



BaP by HPLC - How a lab integrates this peak can have a two-fold effect on calculated yield

Cigarette (µg/cig)	*Mean*	*r*	*R*	*R%*
2R4F	7.3	1.3	2.5	35
A	1.8	0.5	1.0	56
B	5.3	1.1	2.5	48
C	6.5	1.1	2.2	34
D	7.8	1.5	2.9	37
E	8.7	1.4	2.7	31
F	14.1	2.3	5.9	42

Tobacco-Specific Nitrosamines (TSNAs)

- **Several collaborative studies between 1999 and 2005**
  - ✓ Tar yields / puff numbers and conditioning differences were minimal
  - ✓ GC-TEA methodology was most widely used providing sufficient laboratories for collaborative studies under ISO smoking
  - ✓ Only one or two labs used LC-MS/MS at that time
  - ✓ Clean-up procedure was required / several methods investigated and targeted method optimised
- **CRM Collaborative study involved 9 laboratories for NNK, NNN, NAT, NAB**
  - ✓ NAT and NAB data not shown
  - ✓ CRM 63 published (2005)

Cigarette (µg/cig)	*NNN Mean*	*r*	*R*	*R%*
2R4F	146	11	32	22
A	180	29	45	25
B	274	54	90	33
C	42	10	22	53
D	11	3	5	51
E	26	7	15	57
F	85	12	46	54
Cigarette (µg/cig)	*NNK Mean*	*r*	*R*	*R%*
2R4F	141	16	44	31
A	88	13	53	60
B	202	37	146	73
C	36	8	23	65
D	5	2	6	109
E	23	7	12	53
F	52	9	23	44

CORESTA Study 2005-2006

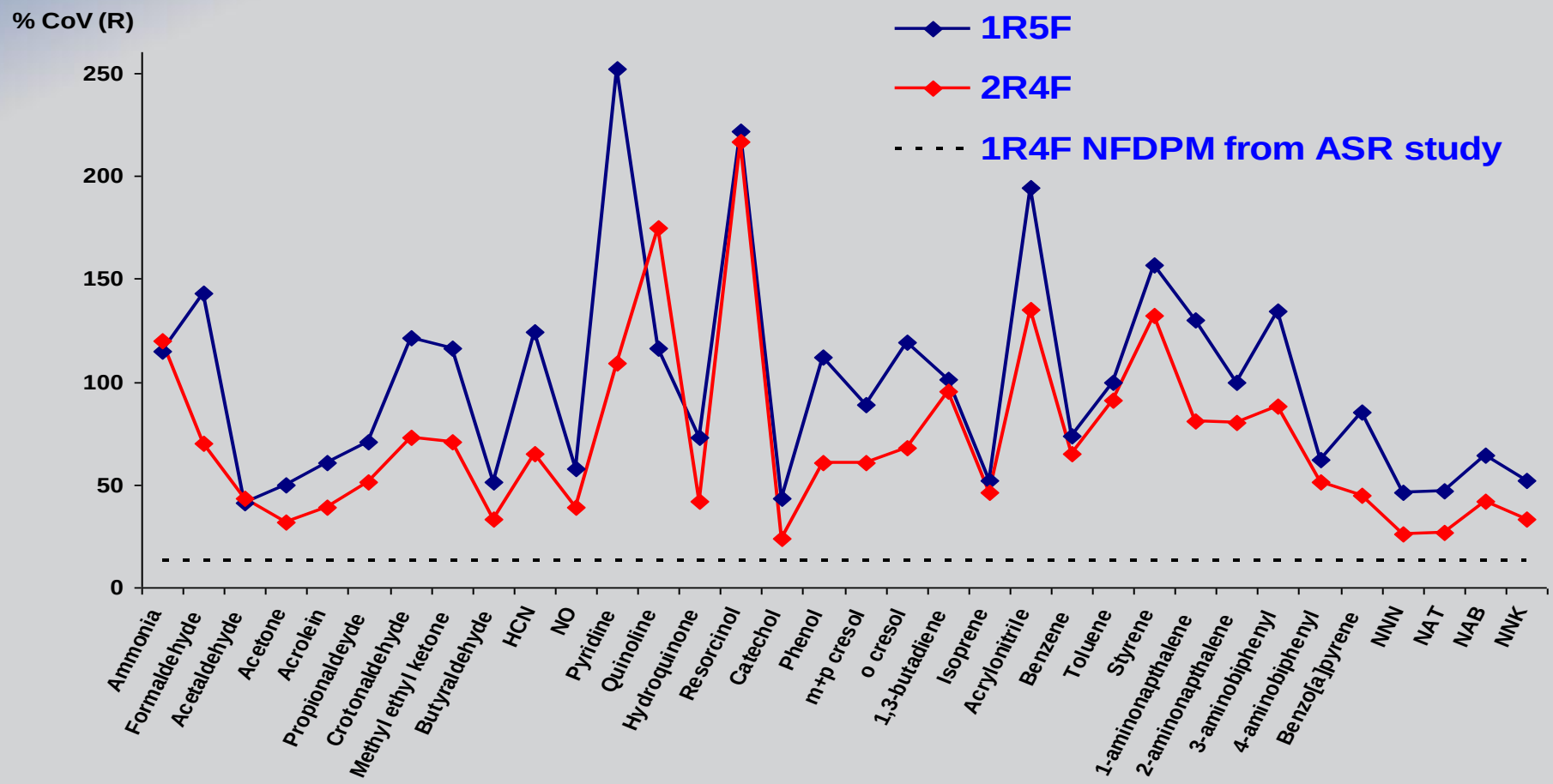
- **Recognised that provision of CORESTA recommended methods**
  - ✓ Was being criticised internally and going much slower than expected
  - ✓ That it was difficult to obtain low levels of between-laboratory variability

- **A study set up allowing individual laboratories to carry out analyses using their preferred and internally validated methods**
  - ✓ Across a wide range of smoke components (based on Hoffmann list)
  - ✓ Metals and bases not included due to insufficient number of participants
  - ✓ 2R4F and 1R5F cigarettes studied / 19 laboratories participated
  - ✓ Questionnaires circulated to compare details of individual methodologies
  - ✓ Published in 2009 (*Beiträge*)

- **Results indicated which analytes would benefit most from further studies**
  - ✓ Some data was so variable between laboratories that it was not possible to even differentiate between the two reference cigarettes
  - ✓ Variability was due to the broad range of methods and method weaknesses or their application in certain laboratories
  - ✓ Work allowed some guidance for future study priorities and for the choice of recommended methodologies
  - ✓ Selected Volatiles / Aromatic Amines and Carbonyls were prioritised

CORESTA Study 2005 - 2006

- ✓ R is much higher for Hoffmann analytes than for NFDPM
- ✓ R is higher for low tar products



Aromatic Amines

- **Joint experiment in 2007**
  - ✓ 18 labs investigated factors in methodology that were potential sources of the high variability previously observed
- **Aromatic amine results showed:**
  - ✓ Internal standard should be added directly after extraction from the filter pad
  - ✓ Beneficial to use both an aminonaphthalene and an aminobiphenyl internal standard
  - ✓ Amine derivative type (PFPA or HFBA) and derivatisation time appeared to have minimal effect compared to the overall variability (method not yet progressed to CRM)
  - ✓ Low inter-lab variability may not be possible to achieve for such analytes measured in ng/cig quantities
- **Work published in 2010 (*Beiträge*)**
  - ✓ To provide guidance towards any future CRM

Selected Volatiles

- **Joint Experiment and Collaborative Study (2008-9) for 5 selected volatiles**
  - ✓ **19 laboratories cold-trapped volatiles after Cambridge filter collection if TPM under ISO smoking**
  - ✓ **Group investigated and discussed a range of factors; e.g.,**
    - trapping efficiencies / trap connection materials / choice of IS / comparison with Tedlar bags / adsorbent traps / chromatographic separations / effect of filter pad / frit coarseness / dead volumes / smoking machine type / questionnaires filled in to provide details and comparisons on various aspects
- **CRM 70 (2010) + 2 papers submitted for publication (2011) to provide additional guidance**
- **High data variability especially for low tar products and for butadiene and acrylonitrile**

Cigarette (µg/cig)	*1,3-Butadiene Mean (R%)*	*Isoprene Mean (R%)*	*Acrylonitrile Mean (R%)*	*Benzene Mean (R%)*	*Toluene Mean (R%)*
1	33 (75)	216 (41)	10.2 (41)	39 (38)	58 (47)
2	32 (78)	256 (42)	5.3 (50)	32 (41)	45 (47)
3	33 (69)	245 (42)	7.5 (46)	35 (39)	49 (48)
4 low tar	8 (93)	58 (53)	1.0 (110)	7 (70)	9 (116)
5	39 (72)	281 (43)	6.3 (49)	29 (48)	37 (55)
CM6	60 (35)	553 (36)	12.3 (48)	60 (35)	85 (48)
1R5F	12 (67)	120 (62)	2.1 (60)	14 (50)	19 (54)
3R4F	41 (71)	362 (37)	8.6 (42)	42 (37)	65 (48)

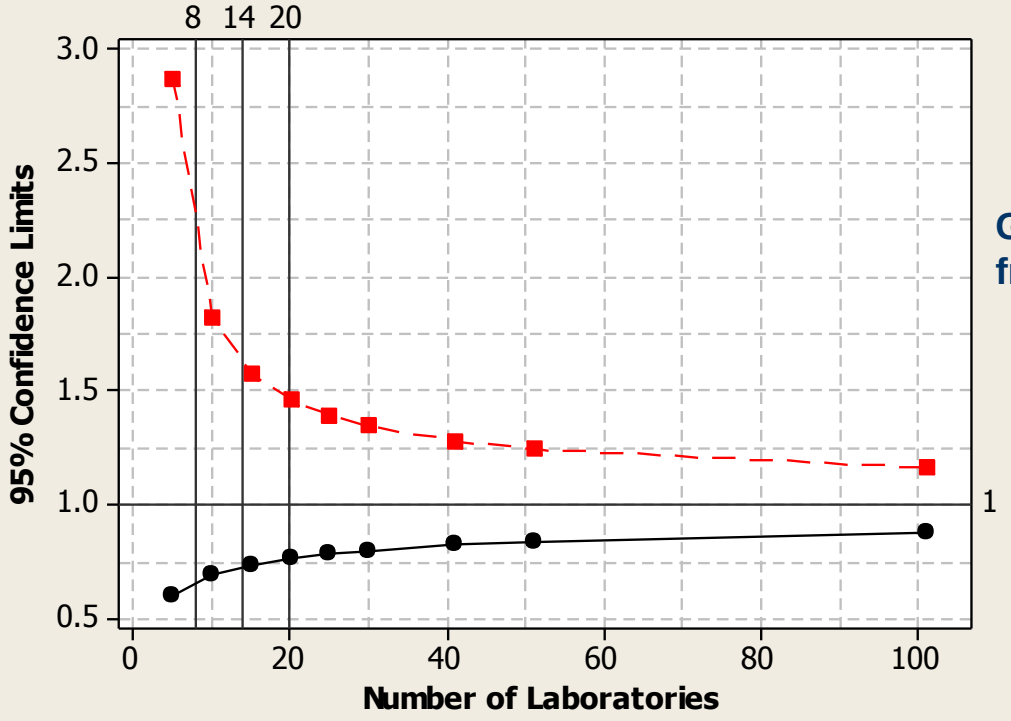
Carbonyls

- **Collaborative Study on 8 carbonyls in 2010**
  - ✓ **15 laboratories trapped carbonyls in an impinger under ISO smoking and derivatised in an acid solution of DNPH followed by quantification by HPLC-DAD or HPLC-UV**
  - ✓ **A range of factors discussed and analysed in detail; e.g.,**
    - effect of smoking machine / measurement of total stereo isomers / inclusion or not of Cambridge Filter in the setup / adjustment for puff volume effects caused by traps
- **CRM available in mid 2011 + 1 paper published (*Beiträge*) to provide additional guidance notes**
- **High variability noted especially for low tar products and for crotonaldehyde, formaldehyde**
  - data for butyraldehyde, MEK and propionaldehyde obtained but not shown

Cigarette (µg/cig)	*Acetaldehyde Mean (R%)*	*Acetone Mean (R%)*	*Acrolein Mean (R%)*	*Formaldehyde Mean (R%)*	*Crotonaldehyde Mean (R%)*
1	496 (41)	199 (50)	42 (57)	15 (90)	17 (89)
2	338 (41)	144 (58)	30 (60)	8 (79)	8 (128)
3	445 (29)	171 (50)	40 (51)	23 (76)	14 (109)
4 low tar	86 (54)	37 (109)	6 (73)	2 (126)	1 (139)
5	516 (35)	182 (49)	45 (58)	28 (81)	12 (129)
CM6	646 (33)	251 (41)	63 (45)	43 (67)	21 (113)
1R5F	141 (61)	62 (84)	10 (87)	3 (122)	2 (138)
3R4F	538 (33)	206 (48)	48 (50)	19 (69)	13 (134)

Lab Numbers for Robust Studies

- ✓ For 20 labs the upper 95% CL is 1.5 and lower 95% CL is 0.76 (i.e., for a 'true' among-laboratory SD of 1)
- ✓ SD could be over-estimated by almost 50% or under-estimated by almost 25%
- ✓ This is not perfect but is appreciably better than for 8 labs for which the SD could be over-estimated by 100% or under- estimated by 66%
- ✓ Most CORESTA studies have >15 participating labs; many have >30 labs



Graph extracted from ISO 5725

The above 95% CLs are for a 'true' between laboratories SD = 1

Participating Laboratories

- ✓ **Number of laboratories (countries) has expanded as experience has widened**
- ✓ **Industry consolidation has also led to decrease due to rationalisation**

Austria Tabak – JTI (Austria)	BAT, Product Centre Europe (Germany)
BAT, Souza Cruz (Brazil)	Imperial Tobacco – Reemtsma (Germany)
Rothmans Benson and Hedges (Canada)	Philip Morris Research Laboratories (Germany)
Labstat International (Canada)	CVS (Govt. Chemist) (Germany)
Zhengzhou Research Institute, CNTC (China)	PT HM Sampoerna (Indonesia)
China National Tobacco Quality Supervision and Test Centre, Zhengzhou (China)	FCPS Authority (Govt. Chemist) (Netherlands)
Shanghai Tobacco, Beijing (China)	PMI Research and Development (Switzerland)
China Tobacco Guizhou Industrial Co Ltd (China)	Thailand Tobacco Monopoly (Thailand)
China Tobacco Zhejiang Industrial Co Ltd (China)	Arista Laboratories Europe (UK)
China Tobacco Anhui Industrial Co Ltd (China)	BAT GR&D (UK)
Imperial Tobacco – SEITA (France)	Filtrona Technology Centre (UK)
LTR Industries (France)	Lorillard Tobacco (USA)
Japan Tobacco (Japan)	R J Reynolds (USA)
KT&G (Korea)	Arista Laboratories (USA)

Current Work

- **TSNA Collaborative Study**
  - ✓ **Analysis by LC-MS/MS under both ISO and CI regimes**
  - ✓ **Product choice reflecting tar range across blend types with the widest range of tar / nicotine ratios as can be found in current markets**
  - ✓ **Data will be reported at April, 2011 meeting in Paris**
- **CTP scientists are invited to participate in the study or attend the meeting to discuss results**

Conclusions

❖ Special Analytes Sub-Group

- ✓ Several methods taken to CRMs
- ✓ High levels of inter-laboratory variability observed
- ✓ These levels of variability may be “as good as it gets”
- ✓ Round-table open discussions have provided invaluable insight into causes and ways of reducing (to some extent) inter-laboratory data variability
- ✓ Data between replicates (typically 5) may be precise within one laboratory but inter-laboratory variability is still high even when working to a “standardised method”

Questions?