

# Dossier quality improvement


## ABIM 2019

### Ctgb & HSE CRD

### October 2019

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# Improving quality of active substance dossier Part I: general issues

Anne Steenbergh, Ctgb NL (E-fate)

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# Volkswagen e-Up!



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# Biopesticides

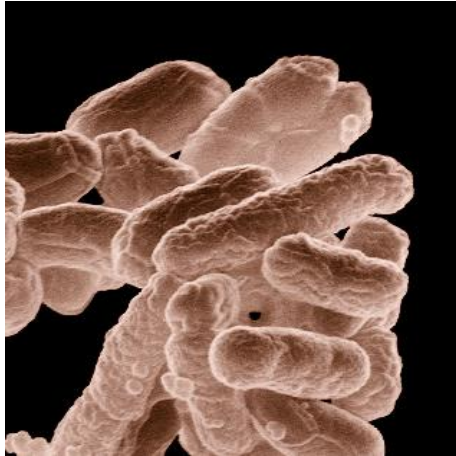


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# Active substance dossier



Botanical



Microorganism

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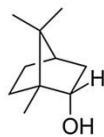


# Botanical general issues

- *Salvia elegans* extract



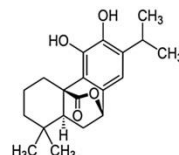
# Botanical general issues



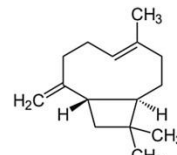
Borneol  
(C<sub>10</sub>H<sub>18</sub>O)



Camphor  
(C<sub>10</sub>H<sub>16</sub>O)



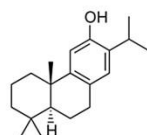
Camosol  
(C<sub>20</sub>H<sub>32</sub>O<sub>4</sub>)



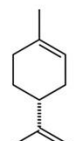
Caryophyllene  
(C<sub>15</sub>H<sub>24</sub>)



Cineole  
(C<sub>10</sub>H<sub>18</sub>O)



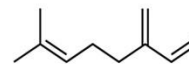
Ferruginol  
(C<sub>20</sub>H<sub>32</sub>O)



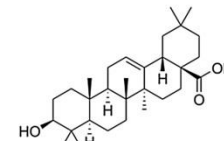
Limonene  
(C<sub>10</sub>H<sub>16</sub>)



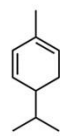
Linalool  
(C<sub>10</sub>H<sub>18</sub>O)



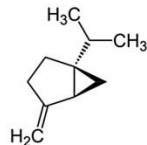
Myrcene  
(C<sub>10</sub>H<sub>16</sub>)



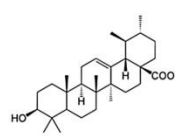
Oleanolic acid  
(C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>)



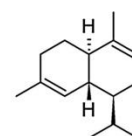
Phellandrene  
(C<sub>10</sub>H<sub>16</sub>)



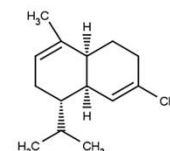
Sabinene  
(C<sub>10</sub>H<sub>16</sub>)



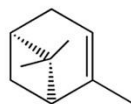
Ursolic acid  
(C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>)



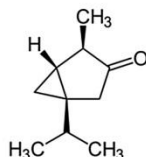
α-Cadinene  
(C<sub>15</sub>H<sub>22</sub>)



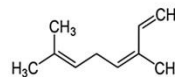
α-Murolene  
(C<sub>15</sub>H<sub>24</sub>)



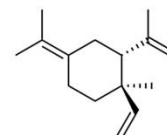
α-Pinene  
(C<sub>10</sub>H<sub>16</sub>)



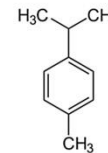
α-Thujone  
(C<sub>10</sub>H<sub>16</sub>O)



β-Ocimene  
(C<sub>10</sub>H<sub>16</sub>)



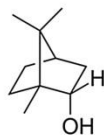
γ-Elementene  
(C<sub>15</sub>H<sub>22</sub>)



p-Cymene  
(C<sub>10</sub>H<sub>14</sub>)

Components of *Salvia officinalis*; Ghorbani & Esmailizadeh 2017

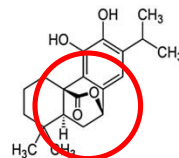
# Botanical general issues



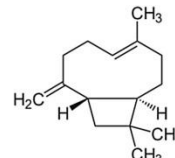
Borneol  
(C<sub>10</sub>H<sub>18</sub>O)



Camphor  
(C<sub>10</sub>H<sub>16</sub>O)



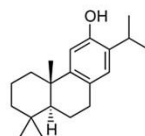
Camosol  
(C<sub>10</sub>H<sub>18</sub>O<sub>2</sub>)



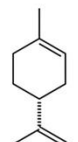
Caryophyllene  
(C<sub>15</sub>H<sub>24</sub>)



Cineole  
(C<sub>10</sub>H<sub>18</sub>O)



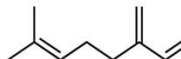
Ferruginol  
(C<sub>20</sub>H<sub>32</sub>O)



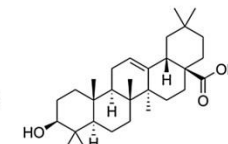
Limonene  
(C<sub>10</sub>H<sub>16</sub>)



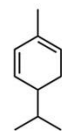
Linalool  
(C<sub>10</sub>H<sub>18</sub>O)



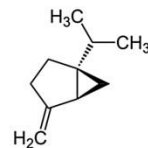
Myrcene  
(C<sub>10</sub>H<sub>16</sub>)



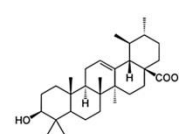
Oleanolic acid  
(C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>)



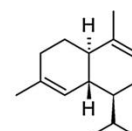
Phellandrene  
(C<sub>10</sub>H<sub>16</sub>)



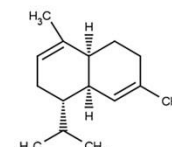
Sabinene  
(C<sub>10</sub>H<sub>16</sub>)



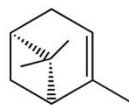
Ursolic acid  
(C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>)



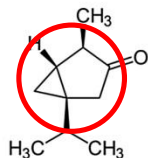
α-Cadinene  
(C<sub>15</sub>H<sub>22</sub>)



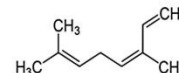
α-Murolene  
(C<sub>15</sub>H<sub>24</sub>)



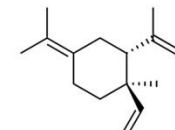
α-Pinene  
(C<sub>10</sub>H<sub>16</sub>)



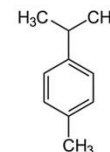
α-Thujone  
(C<sub>10</sub>H<sub>16</sub>O)



β-Ocimene  
(C<sub>10</sub>H<sub>16</sub>)



γ-Elementene  
(C<sub>15</sub>H<sub>22</sub>)



p-Cymene  
(C<sub>10</sub>H<sub>14</sub>)



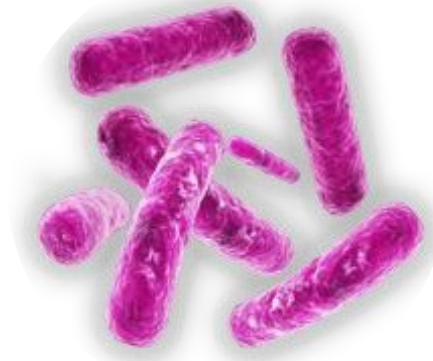
# Botanical general issues

- make overview table for whole dossier
- address all issues, even if you know the compound is not in your active substance
- give information on all components; prevent loose ends



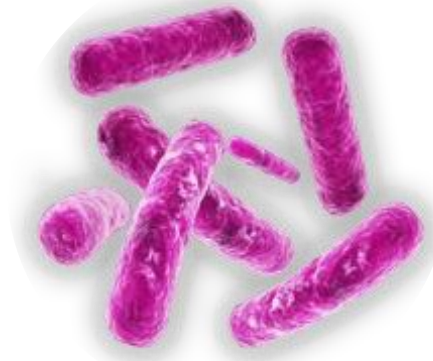
# Microorganism general issues

- *Bacillus amyloliquefaciens*



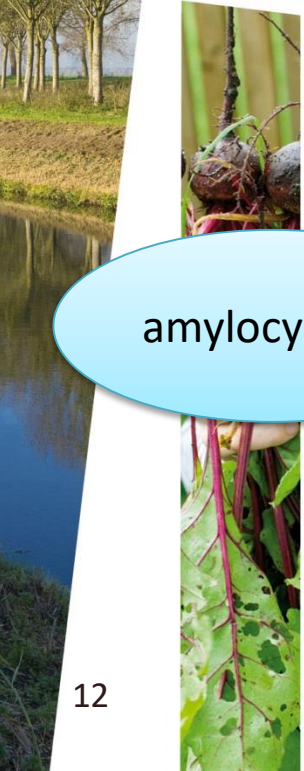
# Microorganism general issues

- *Bacillus* other name?





# Microorganism general issues

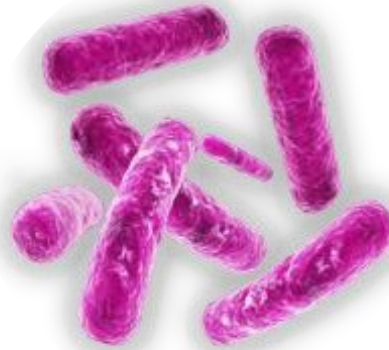


bacilysin

macrolactin

bacillaene

bacillibactin



bacillomycin D

amylocyclicin

difficin

plantazolicin

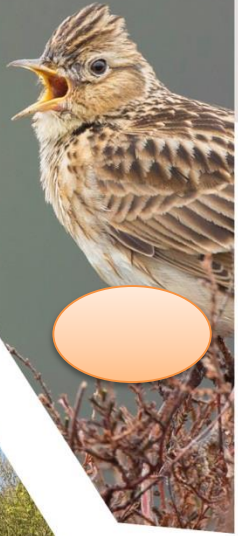
Orphan  
nrps 1

T3pks

fengycin

Ici

# Microorganism general issues



bacilysin

macrolactin

bacillaene

bacillibactin

bacillomycin D

amylocyclicin

difficin

plantazolicin

Orphan  
nrps 1

T3pks

fengycin

Ici

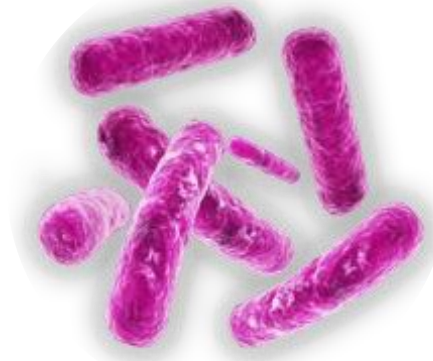
# Microorganism general issues

- list all identified metabolites
- VFDF?
- WGS data: 'no genes were found'
- only subset of metabolites is addressed

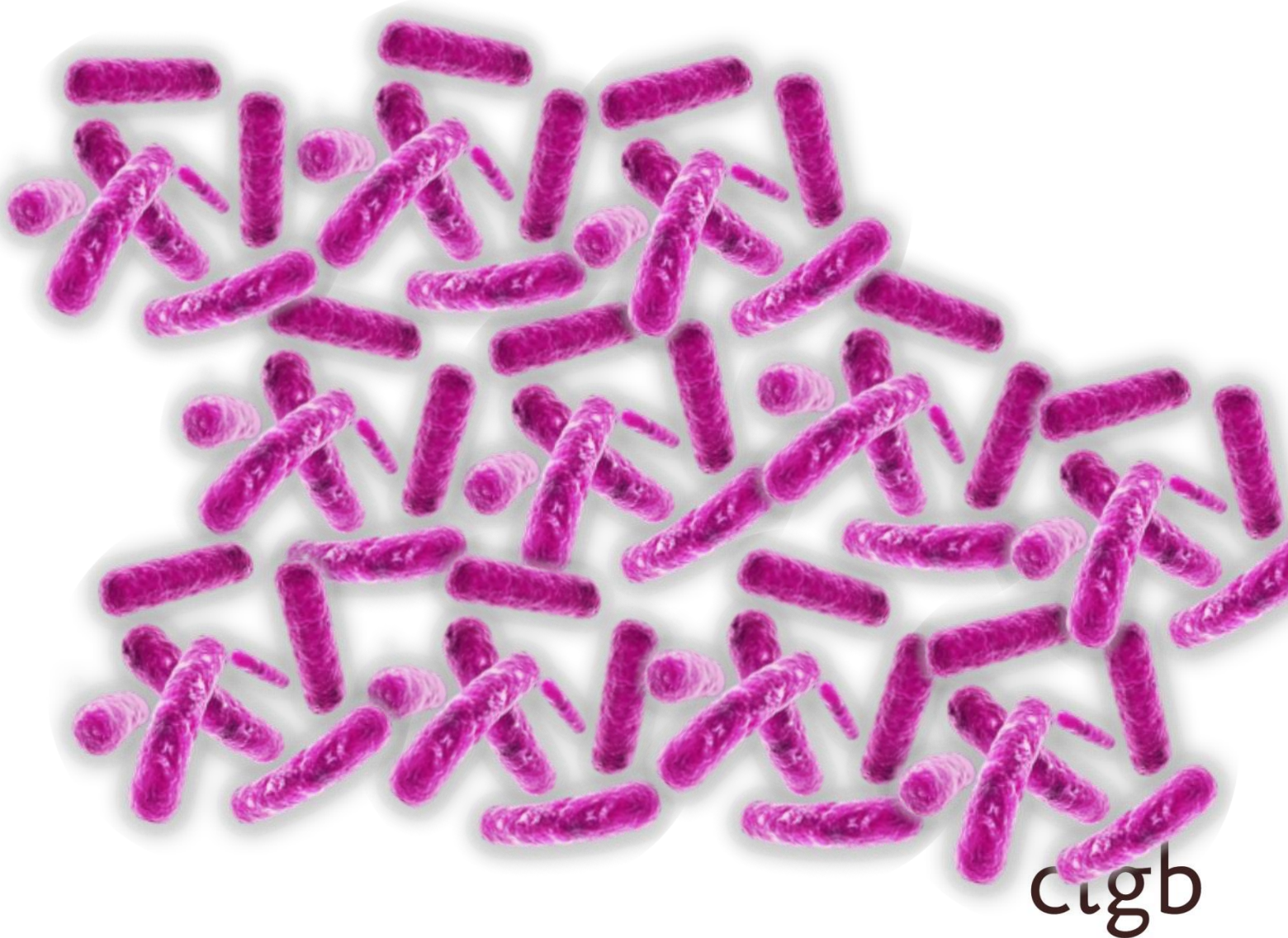




# Microorganism general issues



# Microorganism general issues



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# Efficacy trials (field/greenhouse)



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# Microorganism general issues

- Use taxonomy; explain bridging for every study
- Overview table for metabolites
- Get most out of efficacy trials



# Data requirements

- Should ensure that all information is submitted in dossier to demonstrate safe use
- If not, add information at the best matching data requirement
- prepare overview tables and use cross references to avoid contradictions

